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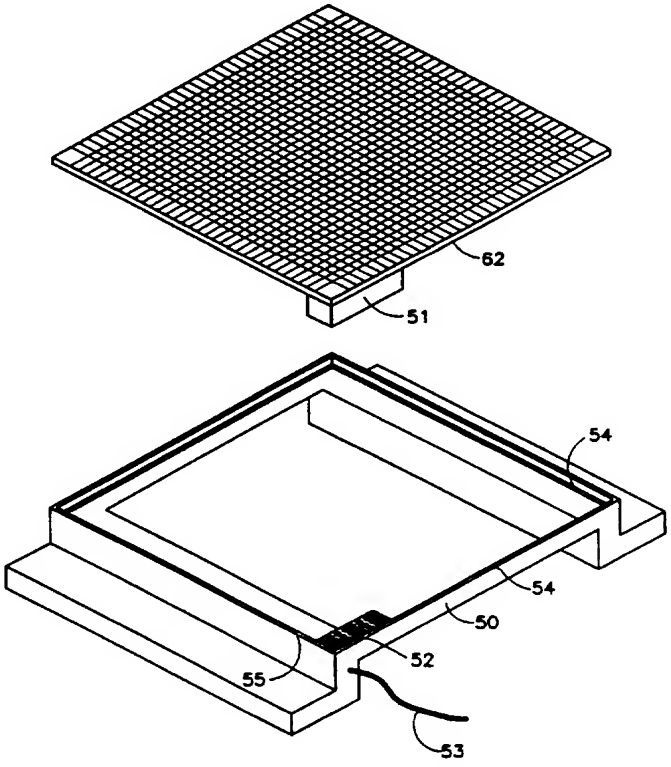

(57) Abstract

A multi-element probe for providing an electrical connection to a tissue surface comprising: a plurality of individual conductive sensing elements (62), each having a front portion suitable for contact with the tissue surface, a plurality of conductive elements (51, 52) providing an electrical connection to the respective individual sensing elements and a partition or spacing separating the individual sensing elements such that when the individual probes contact the tissue surface they are substantially isolated from each other.

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IMPEDANCE IMAGING DEVICES AND MULTI-ELEMENT PROBE

FIELD OF THE INVENTION

The present invention relates to systems for imaging based on the measurement of electrical potentials at an array of points, especially on the skin or other tissue surface of a patient.

BACKGROUND OF THE INVENTION

The measurement of electrical potentials on the skin has many uses. For example, electrocardiograms are derived from measuring the potential generated by the heart of a patient at various points on the skin.

Skin potentials are also measured in apparatus for determining the electrical impedance of human tissue, including two-dimensional (e.g., U.S. Patents 5,063,937, 4,291,708 and 4,458,694) or three-dimensional (e.g., U.S. Patents 4,617,939 and 4,539,640) mapping of the tissue impedance of the body. In such systems an electrical potential is introduced at a point or points on the body and measured at other points at the body. Based on these measurements and on algorithms which have been developed over the past several decades, an impedance map or other indication of variations in impedance can be generated.

U.S. Patents 4,291,708 and 4,458,694 and "Breast Cancer screening by impedance measurements" by G. Piperno et al. Fontiers Med. Biol. Eng., Vol. 2, No. 2, pp 111-117, the disclosures of which are incorporated herein by reference, describe systems in which the impedance between a point on the surface of the skin and some reference point on the body of a patient is determined. These references describe the use of a multi-element probe for the detection of cancer, especially breast cancer, utilizing detected variations of impedance in the breast.

In these references a multi-element probe is described in which a series of flat, stainless steel, sensing elements are mounted onto a PVC base. A lead wire is connected between each of these elements and detector circuitry. Based

on the impedance measured between the elements and a remote part of the body, signal processing circuitry determines the impedance variations in the breast. Based on the impedance determination, tumors, and especially malignant tumors, can be detected.

The multi-element probe is a critical component in this system and in other systems which use such probes. On one hand the individual elements must make good contact with the skin and with the corresponding points on the sensing or processing electronics while also being well isolated from each other. On the other hand, use of gels to improve skin contact carries the risk of cross-talk, dried gel build-up on the elements and inter-patient hygienic concerns.

A paper titled "Capacitive Sensors for IN-Vivo Measurements of the Dielectric Properties of Biological materials" by Karunayake P.A.P. Esselle and Stanislaw S. Stuchly (IEEE Trans. Inst & Meas. Vol. 37, No. 1, p. 101-105) describes a single element probe for the measurement of in vivo and in vitro measurements of the dielectric properties of biological substances at radio and microwave frequencies. The sensor which is described is not suitable for impedance imaging.

A paper entitled "Messung der elektrischen Impedance von Organen- Apparative Ausrüstung für Forschung und klinishe Anwendung" by E. Gersing (Biomed. Technik 36 (1991), 6-11) describes a system which uses single element impedance probes for the measurement of the impedance of an organ. The device described is not suitable for impedance imaging.

A Paper titled "MESURE DE L'IMPEDANCE DES TISSUS HEPATIQUELES TRANSFORMES PAS DES PROCESSUS LESIONELS" by J. Vrana et al. (Ann. Gastroentreol. Hepetol., 1992, 28, no. 4, 165-168) describes a probe for assessing deep tissue by use of a thin injection electrode. The electrode was positioned by ultrasound and specimens were taken for cytological and histological assessment. The electrode was constituted on a

biopsy needle used to take the samples.

A paper titled "Continuous impedance monitoring during CT-guided stereotactic surgery: relative value in cystic and solid lesions" by V. Rajshekhar (British Journal of Neurosurgery (1992) 6, 439-444) describes using an impedance probe having a single electrode to measure the impedance characteristics of lesions. The objective of the study was to use the measurements made in the lesions to determine the extent of the lesions and to localize the lesions more accurately. The probe is guided to the tumor by CT and four measurements were made within the lesion as the probe passed through the lesion. A biopsy of the lesion was performed using the outer sheath of the probe as a guide to position, after the probe itself was withdrawn.

A paper titled "Rigid and Flexible Thin-Film Multi-electrode Arrays for Transmural Cardiac Recording" by J. J. Mastrototaro et al. (IEEE TRANS. BIOMED. ENG. Vol. 39, No. 3, March 1992, 271-279) describes a needle probe and a flat probe each having a plurality of electrodes for the measurement of electrical signals generated in the heart.

A paper entitled "Image-Based Display of Activation Patterns Derived from Scattered Electrodes" by D. S. Buckles et al. (IEEE TRANS. BIOMED ENGR. Vol. 42, No. 1, January 1995, 111-115) describes a system for measurement of electrical signals generated on the heart by use of an array of electrodes on a substrate. The heart with the electrodes in place is viewed by a TV camera and an operator marks the positions of the electrodes on a display. The system then displays the heart (as visualized prior to the placement of the electrodes) with the position markings.

A paper entitled "Development of a Multiple Thin-Film Semimicro DC-Probe for Intracerebral Recordings" by G. A. Urban et al. (IEEE TRANS. BIOMED ENGR. Vol. 37, No. 10, October 1990, 913-917) describes an elongate alumina ceramic probe having a series of electrodes along its length and circumference for measuring functional parameters

(electrical signals) in the brain. Electrophysiological recording, together with electrosimulation at the target point during steriotactic surgery, was performed in order to ensure exact positioning of the probe after stereotactic calculation of the target point. Bidimensional X-Ray imaging was used in order to verify the exact positioning of the electrode tip.

SUMMARY OF THE INVENTION

It is an object of certain aspects of the invention to provide a multi-element probe having improved and more uniform and repeatable contact with the skin with minimal operator expertise and minimal risk of cross-patient contamination.

It is an object of certain aspects of the invention to provide improved inter-element electrical isolation, and to permit sliding of the probe while it is urged against the skin.

It is an object of certain aspects of the invention to provide a relatively inexpensive disposable multi-element probe.

It is an object of certain aspects of the invention to provide a multi-element probe having sufficient transparency to allow for viewing of tissue surface features and to allow for referencing the probe with respect to physical features of or on the skin.

It is an object of certain aspects of the invention to provide a method of distinguishing between artifacts and abnormalities.

It is an object of certain aspects of the invention to provide a system for electrical impedance imaging which simultaneously acquires, uses and preferably displays both capacitance and conductance information.

It is an object of certain aspects of the invention to provide a system for electrical impedance testing of the breast or other body region which provides more accurate information regarding the position of impedance

abnormalities detected in the breast or other region.

It is an object of certain aspects of the invention to provide for electrical impedance testing with a variable spatial resolution.

It is an object of certain aspects of the invention to provide for two dimensional electrical impedance testing giving an indication of the distance of an abnormality from the surface of the skin.

It is an object of certain aspects of the invention to provide apparatus especially suitable for breast impedance measurements.

It is an object of certain aspects of the invention to provide guidance for placement of elongate objects such as biopsy needles, localization needles, fiber optic endoscopes and the like using real time and/or recorded stereotactic images to guide the object.

It is a further object of certain aspects of the invention to provide a biopsy needle having an impedance measuring function to aid in the taking of a biopsy.

It is an object of certain aspects of the invention to provide more direct comparison between the results of electrical impedance maps and the results of optical, ultrasound or other imaging modalities.

It is an object of certain aspects of the invention to provide apparatus and method for indicating, on an anatomical illustration, the location and region from which an impedance image, shown together with the illustration is derived.

It is an object of certain aspects of the invention to provide apparatus which facilitates direct comparison between X-Ray and impedance mammographic images, as for example by superposition of the images.

It is an object of certain aspects of the invention to provide a method of determining a multi-frequency impedance map.

It is an object of certain aspects of the invention to

optimize the impedance mapping utilizing a pulsed voltage excitation.

It is an object of certain aspects of the invention to provide palpation and tactile sensing of an area while simultaneously providing an impedance image of the area.

In general, the term "skin" as used herein means the skin or other tissue of a subject.

There is therefore provided, in accordance with a preferred embodiment of the invention, a multi-element probe for providing an electrical connection to a tissue surface, comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface;

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements; and

a partition separating the individual sensing elements such that, when the sensing elements contact the tissue surface, the sensing elements are substantially electrically isolated from each other.

Preferably, the sensing elements comprise a conductive, viscous gel. Alternatively or additionally, in a preferred embodiment of the invention, the sensing elements comprise a conductive, flexible, solid.

Alternatively or additionally, in a preferred embodiment of the invention the sensing elements comprise a sponge impregnated with a conductive viscous gel.

In a preferred embodiment of the invention, each individual sensing element is located in a well formed by the partition and a substrate underlying the sensing element.

Preferably, the side of the substrate opposite the sensing elements is formed with indentations for aligning the multi-element probe.

In a preferred embodiment of the invention, the well is

formed by embossing the partition on a sheet of material, whereby the un-embossed portion of the sheet forms the substrate underlying the sensing element. Preferably, the indentations are the back of the embossed wells.

In an alternative preferred embodiment of the invention, the well is formed by laminating a grid formed by holes punched in a sheet or formed by extrusion to the substrate.

Alternatively, the well is formed by printing the partitions onto the substrate.

In a preferred embodiment of the invention, there is an electrical connection between a first surface of the substrate inside the well and a second, opposite, surface of the substrate. Preferably the apparatus also comprises an anisotropic conductive sheet overlying the second surface of the substrate.

Alternatively the probe preferably comprises a conductive contact on the second surface of the substrate which is electrically connected to the first surface of the substrate and an adhesive contact overlying the conductive contact.

In a preferred embodiment of the invention, the sensing elements do not extend past the top of the partition or do not extend to the top of the partition.

In a preferred embodiment of the invention the probe includes a cover having a conductive surface facing the front portion of the sensing elements.

There is further provided in accordance with a preferred embodiment of the invention, a multi-element probe for providing an electrical connection to tissue, comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue;

a plurality of conductive elements providing an electrical connection to the respective individual sensing

elements; and

a cover having a surface facing the front portion of the sensing elements, at least that portion of said surface facing the sensing elements being an electrically conductive surface.

Preferably, the cover is formed of a flexible material and wherein, in an unstressed position said electrical conductive surface does not contact said conductive sensing elements. In a preferred embodiment of the invention, the cover is so configured that the surface contacts the sensing elements when a surface of the cover opposite the conductive surface is pressed toward the sensing elements.

In a preferred embodiment of the invention, the cover also includes an area, on the surface facing the individual sensing elements, remote from the individual sensing elements, which is a conductive area electrically connected to said portions facing the sensing elements, the multi-element probe also including a contact electrically connected to the exterior of the probe. Preferably, in an unstressed position said electrical conductive surface does not contact said contact and wherein said cover is so configured that the conductive area contacts the contact when a surface of the cover opposite the conductive surface is pressed toward the sensing elements.

In a preferred embodiment of the invention the probe comprises at least one contact suitable for connection to an external source of electrical energy and also including impedance elements between the conductive surfaces opposite the sensing elements and the contact.

Preferably the cover includes impedance elements between the conductive surfaces opposite the sensing elements and the contact.

There is further provided, in accordance with a preferred embodiment of the invention, a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the side of the substrate opposite the sensing elements is formed with indentations for aligning multi-element probe.

There is further provided, in accordance with a preferred embodiment of the invention, a multi-element probe for the measurement of impedance of tissue, wherein the elements of the probe are sufficiently transparent to allow visualization of tissues beneath the probe when the probe is place in contact with the tissues.

There is further provided, in accordance with a preferred embodiment of the invention, a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements, wherein

the elements of the probe are sufficiently transparent to allow visualization of tissues beneath the probe when the probe is place in contact with the tissues.

Preferably, the sensing elements are formed of a spongy conductive material.

There is further provided, in accordance with a preferred embodiment of the invention a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the

tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the sensing elements are formed of a spongy conductive material.

Preferably, the sensing elements are formed on a flexible surface, whereby the multi-element probe conforms, at least in part, to the tissue.

Preferably, the probe is provided with apertures between sensing elements suitable for the passage of a thin elongate object.

There is further provided, in accordance with a preferred embodiment of the invention, a multi-element probe for providing an electrical connection to a tissue surface comprising:

an array of individual conductive sensing elements spaced over a surface, each element having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the area of the conductive elements comprises less than 50% of the total area encompassed by the array.

There is further provided, in accordance with a preferred embodiment of the invention a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the probe is provided with apertures between sensing elements suitable for the passage of a thin elongate

object.

Preferably, at least a portion of the surface of the probe facing the tissue to be measured is adhesive to the tissue.

There is further provided, in accordance with a preferred embodiment of the invention a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein at least a portion of the surface of the probe facing the tissue to be measured is adhesive to the tissue.

In a preferred embodiment of the invention, the probe further includes:

means for attaching the probe to the finger of a person whereby the person can perform palpative examination concurrently with impedance imaging.

There is further provided, in accordance with a preferred embodiment of the invention a multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a glove having fingers, said sensing elements being attached to the outside of one of the glove at one of the fingers whereby a wearer of the glove can perform palpative examination concurrently with impedance imaging.

There is further provided, in accordance with a preferred embodiment of the invention, a multi-element intermediate device for providing an electrical connection between a multiconductor sensor device and a tissue surface

comprising a plurality of individual conductive sensing element, electrically insulated from each other, each having a front portion suitable for contact with the tissue surface and a back portion detachably matable to the multi-conductor sensor device.

Preferably, the intermediate device includes electrical contacts on the back portion which are electrically connected to the sensing element and which contact a plurality of mating contacts on the multi-conductor sensor device.

There is further provided, in accordance with a preferred embodiment of the invention a catheter or endoscopic probe comprising:

a multi-element probe as described above; and

a fiber optic viewer whose field of view includes at least one surface of the probe when the probe is in contact with the tissue.

There is further provided, in accordance with a preferred embodiment of the invention a catheter or endoscopic probe comprising:

a multi-element probe for providing an electrical connection to a tissue surface, the probe including a plurality of individual conductive sensing elements on a substrate, each sensing element having a front portion suitable for contact with the tissue surface and fiduciary marks visible from an other surface; and

a fiber optic viewer whose field of view includes at least the other surface of the probe.

There is further provided, in accordance with a preferred embodiment of the invention a biopsy needle having:

a leading end for insertion into tissue to undergo biopsy and an elongated outer surface; and

at least one impedance sensing element formed on said outer surface which provides electrical connection to tissue during biopsy.

Preferably, the at least one sensing element comprises a plurality of sensing elements electrically insulated from each other and spaced along the length of the outer surface.

Alternatively or additionally, the at least one sensing element preferably comprises a plurality of sensing elements electrically insulated from each other and spaced along the circumference of the outer surface.

In a preferred embodiment of the invention, at least one sensing element comprises a plurality of sensing elements electrically insulated from each other and forming a matrix of elements spaced along the length and circumference of the outer surface.

There is further provided, in accordance with a preferred embodiment of the invention apparatus for impedance imaging of a breast comprising:

a multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

an electrode adapted for mounting on a side of the breast substantially opposite the multi-element probe; and

a source of electrical energy which provides a voltage between at least a portion of the electrode and at least one element of the probe.

There is further provided, in accordance with a preferred embodiment of the invention apparatus for impedance imaging of a breast comprising:

a multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

an electrode adapted for mounting on a side of the breast substantially opposite the multi-element probe;

an additional electrode adapted for mounting on portion of the body remote from the breast; and

a source of electrical energy which provides a voltage between the additional electrode and at least one element of the probe.

Preferably, the multi-element probe and the electrode adapted for mounting on a side of the breast form respective

parallel planes.

Alternatively, in a preferred embodiment of the invention, the multi-element probe and the electrode adapted for mounting on a side of the breast form two planes at an angle to each other.

Preferably, the apparatus includes a plurality of receivers which measure an electrical signal at the sensing elements.

In a preferred embodiment of the invention, the electrode is adapted for mounting on a side of the breast comprises a second multi-element probe.

Preferably, at least one of the multi-element probes is non-planar to conform to the shape of the breast. The non-planar array can be either rigid or flexible.

Alternatively or additionally at least one of the multi-element probes is flexible so as to conform to the shape of the breast.

There is further provided, in accordance with a preferred embodiment of the invention, apparatus for impedance imaging of a breast comprising:

a first multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

a second multi-element probe adapted for mounting on a side of the breast substantially opposite the multi-element probe; and

a source of electrical energy which alternatively energizes at least some of the elements of one or the other of the first and second multi-element probes by supplying a voltage thereto, wherein the unenergized one of the multi-element probes forms an image based on the voltage applied to the energized probe.

There is further provided, in accordance with a preferred embodiment of the invention apparatus for impedance imaging of tissue comprising:

an impedance probe which produces signals

representative of impedance values sensed by the elements and having fiduciary marks which are visible when the probe contacts the tissue;

an impedance image generator which receives the signals and produces an impedance image;

a video camera which views the probe and tissue and generates a video image; and

a video image processor which receives a video image of the tissue without the probe in place and an image of the tissue with the probe in place, and provides a video image of the tissue with the fiduciary marks and impedance image superimposed thereon.

There is further provided, in accordance with a preferred embodiment of the invention a method of impedance imaging of the breast comprising:

(a) positioning a multi-element probe, comprising a plurality of sensing elements, on one side of the breast;

(b) positioning an electrode on a side of the breast substantially opposite the multi-element probe;

(c) electrifying the electrode; and

(d) measuring a signal at at least some of the elements of the multi-element probe.

There is further provided, in accordance with a preferred embodiment of the invention a method of impedance imaging of the breast comprising:

(a) positioning a multi-element probe, comprising a plurality of sensing elements, on one side of the breast;

(b) positioning an electrode on a side of the breast substantially opposite the multi-element probe;

(c) positioning a second electrode on a portion of the body;

(d) electrifying the second electrode; and

(e) measuring a signal at at least some of the elements of the multi-element probe.

Preferably (b) comprises positioning a second multi-element probe on a side of the breast substantially opposite

the multi-element probe.

There is further provided, in accordance with a preferred embodiment of the invention a method of impedance imaging of the breast comprising:

positioning a first multi-element probe, comprising a plurality of sensing elements, on one side of the breast;

positioning a second multi-element probe on a side of the breast substantially opposite the multi-element probe;

electrifying fewer than all of the plurality of sensing elements of the second multi-element probe; and

measuring a signal at at least some of the elements of the first multi-element probe.

There is further provided, in accordance with a preferred embodiment of the invention a method for guidance in the placement of an elongate element in a region of a subject comprising:

(a) inserting the elongate element into tissue, said element including a plurality of impedance measuring sensing elements thereon;

(b) measuring the impedance between the plurality of sensing elements and an electrode in contact with the subject; and

(c) guiding the element to a desired position having defined impedance properties in response to measurements of impedance made in (b).

Preferably the method also includes:

imaging the region of the subject including the elongate element and generating an image thereof;

receiving the image and the measurements of impedance made in (b) and superimposing a representation of the impedance measurements on the image of the elongate element and surrounding tissues; and

displaying said superimposed images.

In a preferred embodiment of the invention the outer surface of the elongate element is formed with a matrix of impedance measuring elements each measuring the tissue

impedance in a direction generally perpendicular to the element and the display indicates a guiding direction for the elongate element based on the impedance measurements.

There is further provided, in accordance with a preferred embodiment of the invention, a method for guidance in the placement of an elongate element in portion of a patient comprising:

forming a first two-dimensional impedance image of at least a part of said portion from a given direction;

forming second a two dimensional impedance image of at least a part of the portion using a multi-element impedance probe placed at a known angle to the plane of the first image;

inserting the elongate element between elements of the multi-element probe; and

guiding the elongate element to a point at which a biopsy is to be taken at least partially under the guidance of the first and second two dimensional images.

Preferably, the elongate element is inserted into the body through a hole in an array of impedance probe elements and including:

providing a two-dimensional impedance image based on signals received by the array;

guiding the elongate element based on the two-dimensional image; and

determining the desired depth of the elongate element based on impedance signals received from the impedance measuring elements on the elongate element.

There is further provided, in accordance with a preferred embodiment of the invention, a method comprising:

providing an impedance measurement system including a multi-element probe attached to at least one finger of an examiner; and

providing an indication of impedance which is generated on the basis of signals detected by said elements, whereby both a tactile and impedance indication of tissue being

examined are simultaneously acquired.

There is further provided, in accordance with a preferred embodiment of the invention, a method for improving the sensitivity of impedance imaging comprising:

contacting tissue with a multi-element probe;

contacting a different portion of tissue with at least one electrode;

exciting the at least one electrode with a pulsed voltage;

measuring signals, responsive to said pulsed voltage at at least a plurality of the elements of the probe;

computing the real and imaginary parts of an admittance represented by said voltage and signals for a plurality of frequencies at a plurality of said elements; and

choosing at least one frequency as a measurement frequency which gives a large difference for said measures at s elected different elements of the probe.

There is further provided, in accordance with a preferred embodiment of the invention, a method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

manipulating the tissue underlying the probe while the probe remains in stationary contact with the surface of the tissue; and

identifying as a non-artifact those impedance deviations which shift in the direction of the manipulation on the impedance map.

There is further provided, in accordance with a preferred embodiment of the invention, a method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

moving the probe along the surface of the tissue; and

identifying as an artifact those impedance deviations which remain stationary or disappear in the impedance map when the probe is moved.

There is further provided, in accordance with a preferred embodiment of the invention, a method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

moving the probe together with the tissue; and

identifying as a fixed artifact those impedance deviations which move on the impedance map, in the opposite direction from the movement of the probe and the tissue.

There is further provided, in accordance with a preferred embodiment of the invention, a method of displaying impedance imaging information comprising:

displaying at least one impedance image of a region; and

displaying an indication of the imaged region on a representation of the physiology of the patient.

Preferably the display method includes:

simultaneously displaying both a capacitance and a conductance map of the same region.

There is further provided, in accordance with a preferred embodiment of the invention, a method of displaying impedance imaging information comprising:

displaying a capacitance map of a region; and

simultaneously displaying a conductance map of the same region.

There is further provided, in accordance with a preferred embodiment of the invention, a method of displaying impedance imaging information comprising:

computing maps of a plurality of imaging measures; and

simultaneously displaying the measures.

There is further provided, in accordance with a preferred embodiment of the invention, a method of

displaying impedance information comprising:

computing a plurality of maps of at least one imaging measure at a plurality of frequencies; and

simultaneously displaying the maps.

There is further provided, in accordance with a preferred embodiment of the invention, a method of differentiating a suspected carcinoma from a suspected atypical hyperplasia comprising:

comparing a capacitance map of a region to a conductance map of the same region;

classifying a deviation from the surroundings as a suspected atypical hyperplasia if at some frequency less than 500 Hz the capacitance value is lower than that of the surroundings and the conductance value is higher than that of the surroundings; and

classifying a deviation from the surroundings as a suspected cancer if at some frequency less than 500 Hz both the capacitance value and the conductance value are higher than that of the surroundings.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be more fully understood and appreciated from the following detailed description, taken in conjunction with the drawings in which:

Fig. 1 is an overall view of an impedance mapping system especially suitable for breast impedance mapping in accordance with a preferred embodiment of the invention;

Fig. 2 is a perspective view of an imaging head suitable for breast impedance mapping in accordance with a preferred embodiment of the invention;

Figs. 3A and 3B show partially expanded views of two preferred probe head configurations suitable for use in the imaging head of Fig. 2;

Fig. 4 is a top view of a portion of a multi-element probe in accordance with a preferred embodiment of the invention;

Fig. 5A is a partial, partially expanded cross-sectional side view of the probe of Fig. 4 along lines V-V, suitable for the probe head configuration of Fig. 3B;

Fig. 5B is a partially expanded cross-sectional side view of an alternative probe in accordance with a preferred embodiment of the invention;

Fig. 5C shows an alternative embodiment of a multi-element probe, in accordance with a preferred embodiment of the invention;

Fig. 6A is a perspective view of a hand held probe in accordance with a preferred embodiment of the invention;

Fig. 6B shows a partially expanded bottom view of the probe of Fig. 6A, in accordance with a preferred embodiment of the invention;

Fig. 7A is a perspective view of a fingertip probe in accordance with a preferred embodiment of the invention;

Fig. 7B shows a conformal multi-element probe;

Fig. 8 shows an intra-operative probe used determining the position of an abnormality in accordance with a preferred embodiment of the invention;

Fig. 9 shows a laparoscopic probe in accordance with a preferred embodiment of the invention;

Fig. 10 shows a biopsy needle in accordance with a preferred embodiment of the invention;

Fig. 11A illustrates a method of using the biopsy needle of Fig. 10, in accordance with a preferred embodiment of the invention;

Fig. 11B illustrates a portion of a display used in conjunction with the method of Fig. 11A;

Fig. 11C shows a biopsy guiding system in accordance with a preferred embodiment of the invention;

Fig. 11D shows a frontal biopsy guiding system in accordance with a preferred embodiment of the invention;

Fig. 11E shows a lateral biopsy guiding system in accordance with a preferred embodiment of the invention;

Fig. 12 shows, very schematically, the inter-operative probe of Fig. 8 combined with a video camera use to more effectively correlate an impedance measurement with placement of the probe.

Fig. 13 illustrates a laparoscopic probe according to the invention used in conjunction with a fiber-optic illuminator-imager;

Fig. 14 illustrates a display, according to a preferred embodiment of the invention showing both capacitive and conductance images illustrative of atypical hyperplasia;

Fig. 15 illustrates a display, according to a preferred embodiment of the invention showing both capacitive and conductance images illustrative of a carcinoma; and

Fig. 16 illustrates a method useful for verifying a detected local impedance deviation as being non-artifactal and for estimating the deviation;

Figs. 17A and 17B are a block diagram of circuitry suitable for impedance mapping in accordance with a preferred embodiment of the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Reference is made to Figs. 1 and 2 which illustrate an impedance mapping device 10 suitable for mapping the impedance of a breast.

Mapping device 10 includes an imaging head 12, which is described below, which holds the breast and provides contact therewith for providing electrical excitation signals thereto and for receiving resultant electrical signals therefrom. Signals to and from the head are generated and received by a computer/controller 14 which produces impedance maps of the breast under test for display on a monitor 16. The impedance maps may be stored in computer/controller 14 for later viewing or processing or hard copies may be provided by a hard copy device 18 which may be a laser printer, video printer, Polaroid or film imager or multi-imager.

The entire mapping device 10 may be conveniently mounted on a dolly 20 to facilitate placement of the imaging head with respect to the patient.

Fig. 1 also shows a hand held probe 100, described in more detail below, and a reference probe 13.

Fig. 2 shows imaging head 12 in more detail. Head 12 comprises a movable lower plate probe 22 and a stationary upper plate probe 24 which is mounted on a pair of rails 26 to allow the distance between plate probes 22 and 24 to be varied.

Movement of plate probe 22 along rails 26 may be achieved either by a motor (not shown) including suitable protection against over-pressure as is traditional in X-ray breast imaging, or by hand.

Either or both of plate probes 22 and 24 are provided with multi-element probes 28 and 30 respectively, which are described more fully below, which electrically contact the breast with a plurality of sensing elements to optionally provide electrical excitation to the breast and to measure signals generated in response to the provided signals.

Alternatively, electrical excitation to the breast is provided by reference probe 13 which is placed on the arm, shoulder or back of the patient, or other portion of the patient.

In practice, a breast is inserted between probes 28 and 30 and plate probe 24 is lowered to compress the breast between the probes. This compression reduces the distance between the probes and provides better contact between the sensing elements and the skin of the breast. Although compression of the breast is desirable, the degree of compression required for impedance imaging is much lower than for X-Ray mammography, and the mapping technique of the present invention is typically not painful.

Alternatively or additionally, the probes are curved to conform with the surface of the breast.

Head 12 is provided with a a pivot (not shown) to allow for arbitrary rotation of the head about one or more of its axes. This allows for both medio-lateral and cranio-caudal maps of the breast to be acquired, at any angular orientation about the breast. Preferably, head 12 may be tilted so that the surfaces of plate probes 22 and 24 are oriented with a substantial vertical component so that gravity assists the entry of the breast into the space between the maximum extent and to keep it from inadvertently falling out. This is especially useful when the patient leans over the plates so that her breasts are positioned downwardly between the plate probes.

Furthermore, in a preferred embodiment of the invention, one or both of probes 28 and 30 may be rotated about an axis at one end thereof, by a rotation mechanism 27 on their associated plate probes 22 or 24, such as is shown in Fig. 2 for probe 28. Additionally or alternatively, probes 28 and/or 30 may be slidable, as for example along members 31.

Such additional sliding and rotating flexibility is useful for providing more intimate skin contact of the

probes with the breast, which has a generally conical shape. Furthermore, such flexibility allows for better imaging of the areas of the breast near the chest wall or the rib cage, which are extremely difficult to image in x-ray mammography.

Figs. 3A and 3B show partially expanded views of two probe head configurations suitable for use in the imaging head of Fig. 2, in accordance with preferred embodiments of the invention.

In the embodiment of Fig. 3A, a preferably removable multi-element probe 62, which is described below in more detail, is attached to a probe head base 50 via a pair of mating multi-pin connectors 51 and 52. A cable 53 couples connector 52 to computer 14. When multi-element probe 62 is inserted into base 50 (that is to say, when connector 51 is fully inserted into connector 52), the relatively stiff bottom of probe 62 rests on ledges 54 formed in the base, such that the surface 55 of the base and the surface of element 62 are preferably substantially coplanar.

In the embodiment of Fig. 3B, a series of contacts 82 are formed on base 50 and a disposable multi-element probe 62' is attached to the contacts as described below with reference to Fig. 5A and 5B. Cable 53 couples the contacts to computer 14.

Figs. 4, 5A and 5B show top and side views of a portion of multi-element probe 62' and contacts 74, while Figs. 5A and 5B show a partially expanded cross-sectional side view of probe 62' along lines V-V. While the embodiment shown in Figs. 4, 5A and 5B is especially suitable for the probe head configuration of Fig. 3B, much of the structure shown in these figures 5 is common to multi-element probes used in other configurations described herein.

As shown in Figs. 4, 5A and 5B, disposable multi-element probe 62' preferably incorporates a plurality of sensing elements 64, separated by separator or divider elements 66.

As shown more clearly in Figs. 5A and 5B, sensing

elements 64, comprise a bio-compatible conductive material (for example Neptrode E0751 or Neptrode E0962 Hydrogel distributed by Cambrex Hydrogels, Harriman, NY) such as is sometimes used for ECG probes in a well 70 formed by a first, front, side of a mylar or other flexible, non-conducting substrate 68, such as a thin mylar sheet and the divider elements 66. A suitable thickness for the mylar sheet is approximately 0.2 mm for probe 62'. The substrate is preferably pierced in the center of each well. The hole resulting from the piercing is filled with a conducting material which is also present on the bottom of well 70 and on a second, back, side of substrate 68 to form a pair of electrical contacts 72 and 74 on either side of the substrate and an electrically conducting feed-through 76 between the pair of contacts. As shown, a separate contact pair and feed-through is provided for each sensing element.

Alternatively, the substrate may be formed of any suitable inert material including plastics such as polyethylene, polypropylene, PVC, etc.

Wells 70 may be formed in a number of ways. One method of forming the wells is to punch an array of square holes in a sheet of plastic, such as polypropylene, which is about 0.2-1mm thick. This results in a sheet containing only the divider elements. This sheet is bonded to substrate 68 which has been pre-pierced and in which the contacts and feed-throughs have been formed. Another method of forming the wells is to emboss a substrate containing the contacts and feed-throughs to form divider elements in the form of ridges which protrude from the substrate as shown in Fig. 5B. Yet another method of producing the wells is by printing the well walls using latex based ink or other bio-compatible material having a suitable firmness and flexibility. Another method of production is by injection molding of the substrate together with the divider elements. And yet another method of producing the wells is by laminating to the substrate a preformed grid made by die cutting the array

of divider elements in a sheet of plastic, injection molding, or other means.

The conductors and feed-throughs may be of any conductive material which will provide reliable feed-through plating of the holes. One method of manufacturing the contacts and holes is by screen printing of the contacts on both sides of the substrate. If conductive paste having a suitable viscosity is used, the paste will fill the hole and form a reliable contact between contacts 72 and 74. Although many conductive materials can be used, non-polarizing conductors, such as silver/silver chloride are preferred. A conductive paste suitable for silk screening the conductors onto the substrate is Pad Printable Electrically conductive Ink No. 113-37 manufactured and sold by Creative Materials Inc., Tyngsboro, MA.

In general contacts 72 and 74 are only 10-200 microns thick and wells 70 are generally filled with conductive viscous gel material or hydrogel material to within about 0.2 mm of the top of the dividing elements. In general, if low separators are used, the hydrogel may be omitted. However, in the preferred embodiment of the invention, the wells are at least partially filled by hydrogel or a similar material.

Hydrogel is available in both UV cured and heat cured compositions. In either case a measured amount of uncured semi-liquid hydrogel is introduced into each well and the hydrogel is cured. Alternatively, the wells are filled with the uncured material and a squeegee which is pressed against the top of the divider elements with a predetermined force is moved across the top of the divider elements. This will result in the desired gap between the top of the hydrogel and the top of the wells.

In an alternative embodiment of the invention, the hydrogel material is replaced by a sponge material or similar supportive matrix impregnated with conductive viscous gel or the well is simply filled with the conductive

gel to the desired height.

During use of the probe, the probe is urged against the skin which is forced into the wells and contacts the hydrogel or alternative conductive material. Optionally, a somewhat viscous conductive gel, such as Lectron II Conductivity Gel (Pharmaceutical Innovations, Inc. Newark, NJ), may be used to improve contact with the skin. In this case, the dividing elements will reduce the conduction between the cells such that the substantial independence of the individual measurements is maintained. Alternatively, the conductive gel may be packaged together with the probe, with the conductive gel filling the space between the top of the hydrogel and the top of the wells. The use of a conductive gel is preferred since this allows for sliding movement of the probe and its easy positioning while it is urged against the skin. The separators substantially prevent the conductive gel from creating a low conductance path between adjoining sensing elements and also keep the hydrogel elements from touching each other when the probe is applied to the skin with some pressure.

In a further preferred embodiment of the invention, the sensing elements are formed of a conductive foam or sponge material such as silicone rubber or other conductive rubber or other elastomer impregnated with silver or other conductive material, as shown in Fig. 5C. Fig. 5C shows the sensing elements without walls 66. Elements which protrude from the substrate as shown in Fig. 5C may achieve substantial electrical isolation from one another by spacing them far enough apart so that do not contact each other in use or by coating their lateral surfaces with insulating material such as polyethylene or other soft non-conductive plastic or rubber.

For relatively short rigid or compressible elements, it has been found that reducing the size of the sensing elements such that no more than 70% (and preferably no more than 50%) of the area of the array is covered is sufficient

to reduce the "cross-talk" between adjoining elements to an acceptable level.

If sufficiently good isolation is achieved between probe elements by their spacing alone, then foam or other elements without hydrogel and without walls 66 may be provided. Sensing elements such as those shown in Fig. 5C conform and mate to uneven surfaces when pressed against tissue.

Multi-element probe 62', which is preferably used for only one patient and then discarded, is preferably removably attached to a probe holder which preferably comprises a printed circuit board 80 having a plurality of contacts 82 corresponding to the contacts 74 on the back of the substrate, each PC board contact 82 being electrically connected to a corresponding contact 74 on the substrate. To facilitate alignment of the matching contacts, an alignment guide 90 is preferably provided on or adjacent to PC board 80 (Fig. 4). This guide may consist of a series of guide marks or may consist of a raised edge forming a well into or onto which the substrate is inserted. Conductors within PC board 80 connect each of the contacts to one of the pins of connector 51, which is preferably mounted on PC board 80.

Alternatively and preferably, as described below with respect to Fig. 6B, the guide may consist of two or more pins located on or near PC board 80, which fit into matching holes in probe 62'.

Alternatively as shown in Fig. 5B, the back side of the embossing of substrate 68 is used as the guide for one or more protruding elements 83 which are preferably mounted on PC board 80. Preferably a plurality of protruding elements are provided to give good alignment of the substrate with the PC board. The elements may run along the periphery of the probe and form a frame-like structure as shown in Fig. 5B or may run between the elements or may take the form of x shaped protuberances which match the shape of the embossing

at the corners of the wells.

Protruding elements 83 may be formed of polycarbonate, acetate, PVC or other common inert plastic, or of a noncorrosive metal such as stainless steel.

A wire 84 is connected to each PC contact 82 and is also connected to apparatus which provides voltages to and/or measures voltages and/or impedances at the individual sensing elements 64, as described below.

In a preferred embodiment of the invention, conductive adhesive spots 86 preferably printed onto the back of the substrate are used to electrically and mechanically connect contacts 74 with their respective contacts 82. Preferably a conductive adhesive such as Pressure Sensitive Conductive Adhesive Model 102-32 (Creative Materials Inc.) is used. Alternatively, the adhesive used for printing the contacts/feed-throughs is a conducting adhesive and adhesive spots 86 may be omitted. Alternatively, pins, which protrude from the surface of PC board 80 and are connected to wires 84 pierce the substrate (which may be pre-bored) and contact the gel or hydrogel in the wells. A pin extending from the substrate may also be inserted into a matching socket in the PC board to form the electrical connection between the sensing element and the PC board. Alternatively, the entire back side of the substrate can be adhered to the printed circuit board surface using an anisotropically conductive thin film adhesive which has a high conductivity between contacts 74 and 82 and which has a low conductivity resulting in preferably many times higher resistance between adjoining contacts than between matching contacts, in practice at least one hundred times different. An example of such adhesive is tape NO. 3707 by MMM Corporation, Minneapolis MN. However, due to the difficulty of applying such material without trapped air bubbles, it may be preferably to apply adhesive only to the contacts themselves. In practice a release liner of polyethylene, mylar or paper with a non-stick surface on one side is

provided on the lower side of the adhesive sheet. This liner protects the adhesive layer prior to connection of the disposable multi-element probe to the probe holder and is removed prior to the connection of the probe to the holder.

Preferably, the impedance between contacts 82 and skin side of the conducting material in the wells should be less than 100 ohms at 1 kHz and less than 400 ohms at 10 Hz.

Impedance between any pair of contacts 82, with the multi-element probe mounted should preferably be greater than 10 kohm at 1 kHz or 100 kohm at 10 Hz.

Another suitable material for producing substrates is TYVEX (DuPont) substrate which is made from a tough woven polyolefin material available in various thicknesses and porosities. If such material having a suitable porosity is used, contacts 72 and 74 and feed-through 76 can be formed by a single printing operation with conductive ink on one side of the TYVEX sheet. Due to the porosity of the TYVEX, the ink will penetrate to the other side of the TYVEX and form both contacts and feed-through in one operation.

For probe 62 in the embodiment of Fig. 3A, substrate 68 is replaced by a relatively rigid PC board which includes conducting wires to attach each of electrical contacts 72 to one of the pins of connector 51 (Fig. 3A) and the rest of the connecting structure of Fig. 5A may be omitted. It should be noted that the choice of using the structure of Figs. 3A or 3B (i.e., probes 62 or 62') is an economic one depending on the cost of manufacture of the probes. While probe 62 is structurally simpler, the disposable portion of probe 62' is believed to be less expensive to manufacture in large quantities. Since it is envisioned that the probes will be used in large quantities and will preferably not be reused, one or the other may be preferable.

The other side of the probe is also protected by a cover plate 88 (Figs. 5A and 5B) which is attached using any bio-compatable adhesive to the outer edges of dividers 66 (Fig. 5A) and/or to the hydrogel, which is preferably

moderately tacky. In one preferred embodiment of the invention, the inner surface of the cover plate 88 is provided with an electrically conductive layer so that the impedance of each sensing element from the outer surface of the hydrogel (or conductive gel) to contact 82, can be measured using an external source. In addition, if a known impedance is connected between the conductive layer and a reference point or a source of voltage, the sensing elements can be tested in a measurement mode similar to that in which they will finally be used.

Alternatively, a film RC circuit or circuits may be printed on the inner surface of plate 88 to simulate an actual impedance imaging situation. Alternatively, plate 88 may be provided with contacts at each sensing location, and circuitry which may simulate a plurality of actual impedance imaging situations. Such circuitry may include external or integral logic such as programmable logic arrays and may be configurable using an external computer interface. The simulation may provide a distinct RC circuit for each sensing element or may provide a sequence of different circuits to each sensing element to simulate the actual range of measurements to be performed using the probe.

Fig. 5B shows a preferred embodiment of cover sheet 88 (indicated on the drawing as 88') and its mode of attachment to both the multi-element sensor and the PC board. In this embodiment a multi-element probe 62" is optionally further attached to PC board 80 by an adhesive frame 210 which may be conductive or non-conductive, and which assists in preventing entry of water or gel under sensor 62". Sensor 62" is preferably further aligned to PC board 80 by one or more holes 222 with one or more pins 204, which are permanently attached to PC board 80 or to a surface adjacent to PC board 80. While pin 204 is shown as being round, using rectangular, triangular, hexagonal pyramidical or other shapes provides additional alignment of the sensor. In general the upper portion of the pin should be curved for

improved electrical contact as described below.

The upper exposed surface of pin 204 is conductive, preferably curved and is preferably connected to a signal reference source by a conductor 202 in PC board 80. Cover sheet 88' is made of a single integral sheet of easily deformable polyethylene, Mylar or other suitable plastic. Cover sheet 88' is preferably removably attached to the upper side of multi-element probe 62" by a continuous frame of adhesive 225, which need not be conductive, but which seals around a lip where cover 88' contacts probe 62" to protect the quality and sterility of array 230 and to maintain the moisture content of any medium filling wells 70. Cover 88' is coated on the side facing probe 62" with a conductive layer 231, such as any of the various metallic coatings, for example, aluminum or the thin film coating described above.

Cover 88' is preferably formed after conductive coating, by embossing, vacuforming or other means, to have depressions 233 in the cover located over corresponding wells 70. The depressions are approximately centered on the center of the wells and held a small distance "$\delta 1$" above the surface of the hydrogel or gel, by means of relatively high sidewalls 226 which are formed at the same time as depressions 233. Furthermore, the surface of cover 88' preferably has a concave shape to match the rounded conductive contact surface of pin 204, from which it is held at a distance "$\delta 2$". Distances $\delta 1$ and $\delta 2$ are selected to minimize unintended physical contact between the conductive inner surface of the cover, the contacts in the wells and pin 204, for example, during storage and handling prior to use, which might cause corrosion over time due to electrochemical processes.

Distances $\delta 1$ and $\delta 2$ are also preferably selected so that application of a nominal force (preferably about one kilogram) against a flat outer surface 232 of cover 88', such as by a weighted flat plate, will establish contact

between the inner coating 231 and the upper surface of pin 204 and with the sensing elements or the gel in the wells.

By establishing this contact, the conductive inner surface 231 is connected, on the one hand to signals source contact 202 and with each sensing element. If the coating is a conductor, the sensing elements are all excited by the signal on line 202; if it is a thin film circuit, the contact is via the thin film circuit. In either event, if line 202 is excited by a signal, the signal will be transmitted to each of the sensing elements, either directly, or via a known impedance.

In either case, the multi-element array can be tested by the system and any residual impedance noted and corrected when the probe is used for imaging. If the residual impedance of a given sensing element is out of a predetermined specification, or is too large to be compensated for, the multi-element probe will be rejected. Furthermore, the computer may be so configured that imaging may only take place after determination of the contact impedance of the sensing elements or at least of verification that the probe impedances are within a predetermined specification.

While pin 204 is shown as being higher than the top of the wells, the pin may be at the same height as the wells, or even below the wells with the cover being shaped to provide a suitable distance "δ2" as described above.

In an alternative embodiment of the invention, the contact surface corresponding to pin 204 is printed on or attached to the surface holding the sensing elements, with contact to the PC board being via a through contact in substrate 68, as for the sensing elements.

In yet another embodiment of the invention, the conductive contact surface associated with pin 204 is on the surface holding the sensing elements adjacent to pin 204. Pin 204 supports this surface and contacts the contact surface via one, or preferably a plurality of through

contacts. Pin 204 is designed to match the contour of the contact surface and preferably, by such matching, to provide additional alignment of the probe on the PC board.

To avoid drying out of the Gel or other potential hazards of limited shelf life, the quality of any of the aforementioned versions of the disposable electrode arrays can be assured by incorporating an identification code, preferably including manufacturer and serial number information and date of manufacture. In a preferred embodiment, the information is coded in a bar code printed on each disposable probe, which is packaged together with at least one other such probe (typically 5-50 probes) in the same packet, which also has the same bar code. A bar code reader, interfaced with the system computer, reads the manufacturing information on the packet and each probe, checking for date and compliance and permitting recording only for a number of patients equal to the number of probes in the packet.

In a preferred embodiment of the invention a bar code may be placed on the individual disposable electrode arrays which can be read by a bar code reader installed in or under the PC board, for example near reference numeral 83 of Fig. 5B.

While the invention has been described in conjunction with the preferred embodiment thereof, namely a generally flat, somewhat flexible structure, suitable for general use and for breast screening, other shapes, such as concave structures (e.g., brassiere cups) or the like may be preferable, and in general the shape and configuration of the detectors will depend on the actual area of the body to be measured. For example cylindrical arrays can be useful in certain situations, for example in intra-rectal examinations of the prostate or colon or inside vessels. In this context, a probe according to the invention is also useful for measurements inside the body, for example gynecological measurements or measurements in the mouth, where the probe

is inserted into a body cavity and contacts the lining of the cavity, and probes having shapes which correspond either flexibly or rigidly to the surface being measured can be used. For example, a multi-element probe in accordance with the invention may be incorporated into or attached to a laparoscopic or endoscopic probe.

Furthermore, sterilized probes can be used in invasive procedures in which the probe is placed against tissue exposed by incision. In this context, the term "skin" or "tissue surface" as used herein includes such cavity lining or exposed tissue surface.

In a preferred embodiment of the invention, PC board 80 and as many elements as possible of probe 62' (or the board of probe 62) are made of transparent or translucent material, so as to provide at least some visibility of the underlying tissue during placement of probe 62. Those elements of the probe and conductors in the PC board, to the extent that they are opaque should be made as small as practical to provide the largest possible view to a technician or clinician to aid in placement of the probe. Furthermore, probe 62 is slidably displaceable when used with the above-mentioned conductive gel to permit moderate lateral adjustment of the probe position, to aid in placement, to ensure good contact between each element and the tissue surface to be measured, and to enable the user to rapidly verify whether detected abnormalities are artifacts due to poor contact or are genuine objects, since artifacts remain stationary or disappear entirely when the probe is moved while genuine objects just move in a direction opposite to the direction of movement of the probe.

The general shape and size of the multi-element probe and the size of the conductive sensing elements will depend on the size of the area to be measured and on the desired resolution of the measurement. Probe matrix sizes of greater than 64 x 64 elements are envisioned for viewing large areas and probes which are as small as 2 x 8 elements can be

useful for measuring small areas. Element size is preferably between 2 mm square and 8 mm square; however, larger sizes and especially smaller sizes can be useful under certain circumstances. For the breast probe 62 described above, 24 x 32 to 32 x 40 elements appear to be preferred matrix sizes.

Fig. 6A shows a perspective view of a hand held probe 100 in accordance with a preferred embodiment of the invention. Probe 100 preferably comprises two probe heads, a larger head 102 and a zoom sensor head 104. A handle 106 connects the sensor heads, houses switching electronics and provides means for holding and positioning the probes. Handle 106 also optionally incorporates a digital pointing device 105 such as a trackball, pressure sensitive button or other such joystick device. Incorporation of a pointing device on the probe enables the operator to control the system and input positional information while keeping both hands on either the probe or patient. As described below, the digital pointing device can be used to indicate the position on the patient's body at which the image is taken.

Fig. 6B shows a partially expanded bottom view of probe 100 of Fig. 6A, in accordance with a preferred embodiment of the invention. Where applicable, like parts of the probes throughout this disclosure are similarly numbered. Starting from the bottom of Fig. 6B, the top half of a housing 108A has a well 110 formed therein. A clear plastic window 112 is attached to the edge of well 110, and a printed circuit on a relatively transparent substrate, such as Kapton, designated by reference 80' (to show its similarity to the corresponding unprimed element of Fig. 5) is placed on window 112. A flexible print cable 114 connects the contacts on printed circuit 62' to acquisition electronics 116. A cable 118 connects the acquisition electronics to the computer. A second similarly constructed, but much smaller zoom sensor probe head is attached to the other end of probe 100. Either of the larger or smaller heads may be used for imaging.

A lower half of housing 108B, encloses electronics 116 and print 80', whose face containing a series of contacts 82', is available through an opening 120 formed in the lower housing half 108B. A mounting frame 122 having two alignment pins 124 holds print 80' in place. Mounting and connecting screws or other means have been omitted for simplification.

A disposable multi-element probe 62', similar to that of Fig. 5 is preferably mounted on the mounting frame to complete the probe.

Fig. 7A is a perspective view of a fingertip probe 130 in accordance with a preferred embodiment of the invention as mounted on the finger 132 of a user. Probe 130 may be separate from or an integral part of a disposable glove, such as those normally used for internal examinations or external palpation. The fingertip probe is especially useful for localizing malignant tumors or investigating palpable masses during surgery or during internal examinations. For example, during removal of a tumor, it is sometimes difficult to determine the exact location or extent of a tumor. With the local impedance map provided by the fingertip probe 130 and the simultaneous tactile information about the issue contacted by the probe, the tumor can be located and its extent determined during surgery. In a like fashion, palpable lumps detected during physical breast (or other) examination can be routinely checked for impedance abnormality.

Fig. 7B shows a flexible probe array 140 which is shown as conforming to a breast being imaged. Probe array 140 comprises a plurality of sensing elements 141 which contact the tissue surface which are formed on a flexible substrate. Also formed on the flexible substrate are a plurality of printed conductors 142 which electrically connect the individual sensing elements 141 to conductive pads on the edge of the substrate. A cable connector 144 and cable 145 provide the final connection link from the sensing elements to a measurement apparatus. Alternatively, the flexible

array may take a concave or convex shape such as a cup (similar in shape to a bra cup) which fits over and contacts the breast.

The flexible substrate is made of any thin inert flexible plastic or rubber, such as those mentioned above with respect to Fig. 5A. Array 140 is sufficiently pliant that, with the assistance of viscous gel or conductive adhesive, the sensor pads are held in intimate contact with the skin or other surface, conforming to its shape.

Fig. 8 shows an intra-operative paddle type probe 140 used, in a similar manner as probe 130, for determining the position of an abnormality in accordance with a preferred embodiment of the invention. This probe generally includes an integral sensing array 143 on one side of the paddle. Preferably, the paddle is made of substantially transparent material so that the physical position of the array may be determined and compared with the impedance map.

Fig. 9 shows a laparoscopic probe 150 in accordance with a preferred embodiment of the invention. Probe 150 may have a disposable sensing array 152 mounted on its side or the sensing array may be integral with probe 150, which is disposable or sterilizable.

Multi-element probes, such as those shown in Figs. 7, 8 and 9, are preferably disposable or sterilizable as they are generally are used inside the patients body in the presence of body fluids. In such situations, there is generally no need or desire for a conductive gel in addition to the probes themselves. Generally, printed sensing elements, such as those printed with silver-silver chloride ink, or sensing elements formed of conductive silicone, hydrogel or of a conductive sponge may be used. While in general it is desirable that the sensing elements on these multi-element probes be separated by physical separators 66 (as shown in Fig. 5), under some circumstances the physical distance between the elements is sufficient and the separators may be omitted.

When performing a needle biopsy, a physician generally relies on a number of indicators to guide the needle to the suspect region of the body. These may include tactile feel, X-Ray or ultrasound studies or other external indicators. While such indicators generally give a reasonable probability that the needle will, in fact take a sample from the correct place in the body, many clinicians do not rely on needle biopsies because they may miss the tumor.

Fig. 10 shows a biopsy needle 154, in accordance with a preferred embodiment of the invention, which is used to improve the accuracy of placement of the needle. Biopsy needle 154 includes a series of sensing elements 156 spaced along the length of the probe. Leads (not shown) from each of these elements bring signals from the elements to a detection and computing system such as that described below. Elements 156 may be continuous around the circumference, in which case they indicate which portion of the needle is within the tumor to be biopsied. Alternatively, the electrodes may be circumferentially segmented (a lead being provided for each segment) so that information as to the direction of the tumor from the needle may be derived when the needle is not within the tumor. Such an impedance sensing biopsy needle can be used, under guidance by palpation, ultrasound, x-ray mammography or other image from other image modalities (preferably including impedance imaging as described herein), taken during the biopsy or prior to the biopsy to improve the accuracy of placement of the needle. In particular, the impedance image from the needle may be combined with the other images in a display. While this aspect of the invention has been described using a biopsy needle, this aspect of the invention is also applicable to positioning of any elongate object such as an other needle (such as a localizing needle), an endoscopic probe or a catheter.

Returning now to Figs. 1-3 and referring additionally to Figs. 11-14, a number of applications of multi-element

probes are shown. It should be understood that, while some of these applications may require probes in accordance with the invention, others of the applications may also be performed using other types of impedance probes.

Fig. 11A shows the use of the biopsy needle in Fig. 10 together with an optional ultrasound imaging head in performing a biopsy. A breast 160 having a suspected cyst or tumor 162 is to be biopsied by needle 154. An ultrasound head 164 images the breast and the ultrasound image, after processing by an ultrasound processor 166 of standard design is shown on a video display 168. Of course, the ultrasound image will show the biopsy needle. The impedance readings from probe 154 are processed by an impedance processor 170 and are overlaid on the ultrasound image of the biopsy needle in the display by a video display processor 172.

In one display mode, the portions, as shown in Fig. 11B of the needle which are within the tumor or cyst and which measure a different impedance from those outside the tumor, will be shown in a distinctive color to indicate the portion of the needle within the tumor or cyst. In a second display mode, the impedance measured will be indicated by a range of colors. In yet a third embodiment of the invention, in which circumferentially segmented sensing elements are employed, the impedance processor will calculate radial direction of the tumor from the needle and will display this information, for example, in the form of an arrow on the display.

The image sensing biopsy needle can also be used with one or more imaging arrays (28, 30) such as those shown in Fig. 6 or Fig. 3B to impedance image the region to be biopsied during the biopsy procedure. Alternatively, at least one of the arrays can be an imaging array of the non-impedance type. In one preferred embodiment, shown in Fig. 11C, the needle is inserted through an aperture (or one of a plurality of apertures) 174 in a multi-element probe which is imaging the region. The region may, optionally, be simultaneously viewed from a different angle (for example at

90° from the probe with the aperture) with an other impedance imaging probe. In the case that both arrays 28 and 30 are impedance imaging arrays, the biopsy needle or other elongate object can either have impedance sensing or not, and the two images help direct it to the region. The probe with one or more apertures is sterile and preferably disposable. This biopsy method is shown, very schematically, in Fig. 11C.

In an alternative preferred embodiment of the invention, only the perforated plate through which the needle or elongate object is passed is an imaging array. In this case the array through which the needle passes give a two dimensional placement of the impedance abnormality while an imaging or non-imaging impedance sensor on the needle gives an indication of when the needle has reached the region of impedance abnormality, as described above.

Alternative guiding systems for frontal and lateral breast biopsy or for guiding an elongate element to a desired impedance region of the body are shown in Figs. 11D and 11E, respectively.

Fig. 11D shows a system for in which two relatively large plate multi-element probes 28, 30 are placed on opposite sides of the desired tissue, shown as a breast 160 of a prone patient 161. Sensor array probes 28 and 30 are held in position by positional controller 181 via rotatable mounts 191. A mount 198 positions a biopsy needle 199 within the opening between probe arrays 28 and 30, and is operative to adjust its height. A suspicious region 183 which is located at positions 184 and 185 on arrays 28 and 30 respectively as described herein, which information is supplied to a CPU 197, which determines the position of the suspicious region for controller 181. The controller then inserts the needle into the suspicious region, for example, to take the biopsy. Biopsy needle 199 is preferably of the type shown in Fig. 10 to further aid in positioning of the needle. As indicated above, this is not required for some

embodiments of the invention.

Alternatively, biopsy needle 199 may be inserted through holes formed between the elements of probes 28 and/or 30 as described above. Furthermore, while automatic insertion of the biopsy needle is shown in Fig. 11D, manual insertion and guidance based on impedance images provided by the probes is also feasible.

Fig. 11E shows a system similar to that of Fig. 11D in which the imaging and biopsy needle insertion is from the side of the breast, rather than from the front. Operation of the method is identical to that of Fig. 11D, except that an additional probe 29 may be provided for further localization of suspicious region 183. Alternatively, one or two of the probes may be substituted by plates of inert material for holding and positioning the breast.

It should be noted that while the breast has been used for illustrative purposes in Figs. 11A through 11E, the method described is applicable to other areas of the body, with necessary changes due to the particular physiology being imaged.

Fig. 12 shows, very schematically, the intra-operative probe of Fig. 8 combined with a video camera 256 to more effectively correlate the impedance measurement with the placement of the probe on the body. An intra-operative probe 140 preferably having a number of optically visible fiduciary marks 146 is placed on the suspect lesion or tissue. A video camera 256 sequentially views the area without the probe and the same area with the probe in place and displays a composite image on a video display 258 after processing by a processor 260. Processor 260 receives the impedance data from probe 140, determines the positions of the fiduciary marks from the video image and superimposes the impedance image on the video image, with or without the probe, which is displayed on display 258.

Fig. 13 shows a laparoscopic or endoscopic probe 250 used in conjunction with a fiber-optic illuminator/imager

252. In this embodiment, the laparoscopic impedance probe, which is formed on a flexible, preferably extendible paddle, is viewed by the illuminator/imager which is preferably a video imager, which is well known in the art. Probe 250 can be either round or flat, depending on the region to be imaged. When the imager views a suspicious lesion or tissue, probe 250 is extended to determine the impedance properties of the lesion. The combination of probe 250 and imager 252 may be incorporated in a catheter 254 or other invasive element appropriate to the region of the body being investigated.

Optically visible fiduciary marks 253 on probe 250 are preferably used to determine the position of probe 250 within the video image of the tissue seen by fiber-optic illuminator/imager 252, in a manner similar to that discussed above with respect to Fig. 12.

In a preferred embodiment of a system using any of the biopsy needle, intra-operative probe, finger tip probe or other embodiments described above, an audible sound proportional to an impedance parameter measured by the needle or other sensor in or on the body is generated by the system computer. This feature may be useful in situations where the probe is placed in locations which are difficult to access visually, such as suspected lesions during surgery. Such an audible sound could include any kind of sound, such as a tone whose frequency is proportional to the measured parameter or similar use of beeps, clicks, musical notes, simulated voice or the like. This feature can also be used for non-surgical procedures such as rectal, vaginal or oral examinations, or other examinations.

Fig. 16 shows methods useful for estimating the depth of a lesion and also for determining if a image contains a true lesion or an artifact.

A breast or other region 160 is imaged by a probe 270, for example, the probe of Figs. 1-3 or Figs. 6A and 6B. The depth of a local impedance deviation can be estimated by

palpating the breast or other region by a finger 272 or a plunger 274. The displacement of the local deviation on the image will be maximized when the palpation is at the same level as the lesion. It should also be understood that, where palpation causes movement of the local deviation on the impedance image, this is an indication that the deviation is "real" and not an artifact.

In a similar manner, application of variable compression to the imaging probe will result in a variation of the distance from the probe to deviation under the probe. This distance variation will cause a corresponding variation in the size and intensity of the deviation, thus helping to verify that the deviation is not artifactal.

Alternatively or additionally, the probe can be moved along the surface of the tissue without moving the tissue. In this case, surface effects will have a tendency to either disappear or to move with the probe (remain stationary in the image) while real anomalies will move, on the image, in the opposite direction from the movement of the probe.

Alternatively or additionally, the probe and the tissue can be moved together without moving the underlying structure (such as the bones). Tissue lesions will remain relatively stationary in the image while bone artifacts will move in the opposite direction.

In operation, a system according to the present invention measures impedance between the individual sensing elements and some reference point (typically the signal source point) at some other place on the body. Generally, in order to produce an interpretable impedance image, the sensing elements in the multi-element probe should detect distortions in the electric field lines due solely to the presence of a local impedance difference between embedded tissue of one type (for example, a tumor) and surrounding tissue of another type (for example, normal adipose tissue).

To avoid distortion in the field lines, the reference point is typically placed far from the sensor array, all

sensing elements are all at ground or virtual ground, and the current drawn by the elements is measured. Since the probe is at ground (an equipotential) the electric field lines (and the current collected by the elements) are perpendicular to the surface of the multi-element probe. In principle, if there are no variations of impedance below the probe, each element measures the integrated impedance below the element. This first order assumption is used in the determination of the position and/or severity of a tumor, cyst or lesion. It is clear, however, that the multi-element probe covers only a portion of even the organ which is being imaged. The area outside the area of the probe is not at ground potential, causing the field lines to bend out at the periphery of the probe, biasing the edge of the impedance image.

To reduce this effect, a conductive "guard ring" is provided around the edge of the imaged area to draw in and straighten the field lines at the edge of the imaged area. This guard ring, if one is desired, can consist of merely ignoring the, presumably distorted, currents drawn by the elements at (or near) the edge of the probe and ignoring the measurements made by these elements.

Furthermore, to possibly reduce the baseline impedance contributed to the local impedance image by tissue between the remote signal source and the region near the probe, an additional reference electrode may be placed on the patient's body relatively near the multi-element probe. For example, if the source is placed at the arm of the patient and the breast is imaged from the front, a reference electrode for sensing a reference voltage can be placed at the front of the shoulder of the patient. The measured impedances are then reduced by the impedance value of the reference electrode. Alternatively, the impedance values of the elements of the multi-element probe are averaged to form a reference impedance, and the display of the impedance map is corrected for this reference impedance.

One way to substantially avoid at least some of the above- mentioned problems is to use the apparatus shown in Figs. 1-3. As indicated above, the apparatus incorporates two probe heads 28 and 30. The breast to be imaged is placed between the probe heads and the breast is compressed by the heads (although generally to a lesser degree than in X-Ray mammography) so that the breast forms a relatively flat volume and fills the region between the probes. It should be noted that, if the current is measured at each of the sensing elements in both probes, then two somewhat different images of the same region are generated. Avoidance of the problems also results when the two multi-element probes are not parallel as described above.

It should be noted that when used on breasts, the images produced by the pair of large, flat probes of Fig. 3 have the same geometric configuration as standard mammograms. Furthermore if used in the same compression orientations, the impedance images can be directly compared to the corresponding mammograms. In one preferred embodiment of the invention, mammograms corresponding to the impedance images to be taken are digitized, using film scanning or other digitization means known in the art, and entered into the system computer. If the mammogram is already digital, such as may be provided by a digital mammogram, the image file can be transferred from the mammogram.

The mammograms and impedance images can be overlaid or otherwise combined to form a single image. Such an image could highlight those areas of the mammogram in which the impedance is particularly low or high. Such a combined image thus presents two independent readouts (impedance and radiographic density) of the same well defined anatomical region in a known geometric orientation, to facilitate interpretation, correlation with anatomy and localization.

It is well known that the resolution of objects in an impedance image is reduced with distance of the object from the probe. Thus, it is possible to estimate the distance of

the object from the two probes based on the relative size of the same object on the two different probes. As indicated above, two opposing views of the breast may be taken. This would provide further localization of the object.

In one mode, the sensing elements of one probe are all electronically floating while the elements of the other probe are at a virtual ground (inputs to sensing electronics), and a remote signal source is used, as previously described. After an image is obtained from the one probe, the roles of the two probes are reversed to obtain an image from the other probe.

Alternatively, if all of the elements of one of the flat probes are electrified to the same voltage and the measuring probe is kept at virtual ground, the currents drawn from and received by the elements of both probes form a two dimensional admittance image of the region between the probes.

In a further preferred embodiment of the invention, one or a few closely spaced sensing elements on one of the probes is electrified, and the others are left floating. This would cause a beam-like flow of current from the electrified elements to the other sensing elements on the other probe. The object would disturb this flow causing impedance variations which are strongest for those elements which are in the path of the current disturbed by the object. If a number of such measurements are made with, each with a different group of electrodes being electrified, then good information regarding the position of the object can be obtained.

In practice, as indicated above, orthogonal views of the breast are taken giving additional position information.

In preferred embodiments of the invention the breast is imaged at a plurality of frequencies and both the real and imaginary parts of the impedance are calculated. The sensitivity of the detection of malignant tissue is a function of frequency, and, for a particular frequency, is a

function of the impedance measure or characteristic used for imaging, for example, real part of the impedance (or admittance), imaginary part of the impedance (or admittance), absolute value of the impedance (or admittance), phase of the impedance (or admittance), the capacitance or some function of the impedance or of admittance components.

In a practical situation, an impedance measure should give the maximum contrast between a malignancy and non-malignant tissue. It is therefore desirable to determine the frequency or combination of frequencies which give maximum detectability and to determine it quickly. One method of determining the frequency is to perform swept frequency measurements and to use the frequency or combination of frequencies which results in the best contrast. Alternatively, a number of images taken at relatively close frequencies can be used. It is believed that for many purposes, at least four samples should be taken in the range between and including 100 and 400 Hz and, preferably, at least one or two additional images are taken at frequencies up to 1000 Hz.

A second method is to use a pulsed excitation and Fourier analysis to determine impedance over a range of frequencies. The optimum frequency or frequencies determined from the swept or pulsed measurement are then used in a single or multiple frequency measurement. A pulse shape which has been found useful in this regard is a bi-polar square pulse having equal positive and negative going pulses of 5-10 millisecond duration and fast rise and fall times.

A number of measures of the impedance, as described below, have been found useful for comparing different areas of the image. Generally, it is useful to display a gray scale or pseudo-color representation of the values of the impedance measure, either on a linear scale or where the square of the impedance measure is displayed. Also useful is an "absorption scale" where the value of an impedance

measure, v, is displayed as:

$$d(v)=(max-1)*(exp(v*(max-1)-1))/(e-1),$$

where max is the maximum normalized value of v. Generally, the display is most useful when the measure is normalized, either by division or subtraction of the minimum or average value of the measure in the display.

Furthermore, the display may be automatically windowed to include only those values of the impedance measure actually in the image, or to include a relative window of selectable size about the average value of the impedance measure. The range of values to be displayed may also be determined using a baseline average value measured at a region remote from irregularities, i.e., remote from the nipple of the breast. Alternatively, the baseline average may be a predetermined average value as measured for a large group of patients. Alternatively, a reference region on the image may be chosen by the user to determine the baseline average to be used for windowing.

While the display may show the exact measure for each pixel as is conventional, for example, in displays of nuclear medicine images, in a preferred embodiment of the invention the display is an interpolated image formed by quadratic or cubic spline interpolation of the impedance measure values. This type of display removes the annoying checkerboard effect of the relatively low resolution impedance image without any substantial loss of spatial or contrast detail.

The measures of impedance which have been found useful for comparing different areas of the image may be grouped as single frequency measures and polychromatic measures.

Single frequency measures include the admittance, capacitance, conductance and phase of the admittance. These measures may be measured at some predetermined frequency, at which the sensitivity is generally high, or at a frequency of high sensitivity determined by a preliminary swept or pulsed measurement.

Polychromatic impedance measures are generally based on a spectral curve based on fitting a set of capacitance (C) and conductance (G) values determined at a plurality of frequencies using linear interpolation, quadratic interpolation, cubic spline, band limited Fourier coefficients, or other methods known in the art.

One polychromatic measure is a spectral width measure. For a give pixel or region of interest the value of both the G and C parameters fall with frequency. The spectral width is the width of the spectrum (to a given percentage fall in the chosen parameter) as compared to the value at some low frequency, for example 100 Hz. If the parameter does not fall by the given percentage in the measured range it is assigned an impedance measure equal to the full measured bandwidth.

A second polychromatic measure is a spectral quotient in which the impedance measure is the ratio of the measured value of G or C parameters at two preset frequencies, which may be user selected, or which may be selected based on the swept or pulsed measurements described above. This measure, as all of the others may be displayed on a per-pixel basis or on the basis of a region of interest of pixels, chosen by the user.

A third type of polychromatic measure is based on a Relative Difference Spectrum determination. In this measure, the capacitance or conductance for a given region of interest (or single pixel) is compared to that of a reference region over the spectrum to determine a numerical difference between the two as a function of frequency. The thus derived Relative Difference Spectrum is then analyzed. For example, a spectral width measure as described above has been found to be a useful measure of abnormalities. Normally the width is measured where the relative difference spectrum passes from positive to negative, i.e., where the C or G is equal to that of the reference region.

A fourth type of polychromatic measure is based on a

Relative Ratio Spectrum determination. This is similar to the Relative Difference Spectrum, except that the ratio of the values between the reference area and the region of interest is used. A spectral width measure can be determined for this spectrum in the same manner as for the Relative difference Spectrum. Normally, the width is measured where the ratio is 1.

A fifth polychromatic measure which may be useful is the maximum of one of the other polychromatic measures, for example, the capacitance, conductance, Relative Difference Spectrum, Relative Ratio Spectrum, etc.

In impedance measurements of the breast in both men and women, normal breast tissue has a low capacitance and conductivity, except in the nipples, which have a higher C and G values than the surrounding tissue with the maximum obtained at the lowest frequency recorded, typically 100 Hz. The nipple capacitance and conductance remains higher than the surrounding tissue up to about 1400 Hz for fertile patients and up to about 2500 Hz for older patients (which is reduced to 1400 Hz for older patients by estrogen replacement therapy). These frequencies represent the normal range of spectral widths for the Relative and Difference Spectra. Tumors can be recognized by very high C and G relative ratio or relative difference values up to 2500 Hz or even higher.

Capacitance and conductance values are measured by comparing the amplitude and phase of the signal received by the sensing elements. Knowing both of these measures at the same points is useful to proper clinical interpretation. For example, as illustrated below in Fig. 14, a region of elevated conductivity and reduced capacitance (especially at relatively low frequencies, most preferably less than 500 Hz, by generally below 2500 Hz and also below 10 kHz) is associated with benign, but typically pre-cancerous atypical hyperplasia while, as shown in Fig. 15, cancer typically has both elevated capacitance and conductivity over, generally,

a wide frequency range, as compared to the surrounding tissue. Proper differential diagnosis is aided by having the frequency samples be close enough together so that changes in the conductivity and capacitance in the low frequency range can be tracked. This also requires the display of both capacitance and conductance or the use of an impedance measure which is based on an appropriate combination of the two.

Methods for calculating C and G are given in the abovementioned US patents 4,291,708 and 4,458,694, the disclosures of which are incorporated herein by reference. A preferred embodiment of the invention takes advantage of the calibration capability inherent in the use of cover plates as shown in Figs. 5A and 5B. It can be shown that if the received waveform is sampled at a fixed spacing, δ, such that N samples are taken in each cycle, then the real and imaginary values of the impedance can be determined as:

$$G = \Sigma(g_n(V_{(n+\frac{1}{2}N)}-V_n),$$

and

$$\omega C = \Sigma(c_n(V_{(n+\frac{1}{2}N)}-V_n),$$

where g_n and c_n are constants determined by a calibration procedure and V_n is the voltage measured at the nth sampling point (out of N). The first sample is taken at zero phase of the reference signal.

One relatively easy way to determine the constants is to perform a series of measurements when cover plate is in contact with the sensing elements as described above and a known impedance is placed between the transmitter and the cover plate. Since N coefficients are required for determining g_n and c_n for each frequency, N values of admittance and N measurements are required. For example, if N=4 (four samples per cycle) four different measurements are taken and the sampled signal values are entered into the above equations to give N equations, which are then solved for the values of the coefficients. The higher the number of

samples, the greater the accuracy and noise immunity of the system, however, the calibration and computation times are increased.

Alternatively, fewer samples are taken and values for a number of measurements are averaged, both in the calibration and clinical measurements to reduce the effects of noise.

Artifactal abnormalities in the impedance image can be caused by such factors as poor surface contact or insufficient conductive coupling on some or all of the sensing elements, the presence of air bubbles trapped between probe and tissue and normal anatomical features such as bone or nipple.

Bubbles can be recognized by their typically lower C and G values compared to background, often immediately surrounded by pixels with much higher C and G. Bubbles can be verified and eliminated by removing the probe from the skin and repositioning it, and or by applying additional conductive coupling agent. Contact artifacts can be determined and accounted for in real time by translating the probe and viewing the image as described above. Artifacts either disappear or remain fixed with respect to the pixels, while real tissue features move, on the image, in a direction opposite from the motion of the probe. Additionally, as described above, if the tissue beneath the skin is physically moved, while the probe and skeletal structure is kept fixed, only real tissue features will move. If the feature remains static, it is either a skin feature or bone.

If as described above, the probe and the tissue are moved together without moving the underlying structure (such as the bones). Tissue lesions and surface effects will remain relatively stationary in the image while bone artifacts will move in the opposite direction, thus distinguishing them from other impedance deviations.

Fig. 14 shows one example of a display, according to a preferred embodiment of the invention. In this display,

capacitance and conductivity images at two positions on a breast are shown, together with an indication of the positions on the breast at which these images were acquired.

In particular, as seen in Fig. 15, the display includes the capability of displaying up to five sets of capacitance and conductance images in the five sets of smaller squares. These images are associated with probe areas indicated as numbers 1-5 on the breast image shown in the display. In practice, the examiner manipulates a joystick or other digital pointing device, such as device 105 shown in Fig. 6A. This device is manipulated until a square is appropriately placed on the breast image. The examiner then presses a button which causes a pair of impedance images to be stored and displayed on the screen in an appropriate square, and the indicated position to be displayed on the physiological (breast) drawing. The small images are numbered from left to right. Preferably, the examiner can scale the physiological image so that the dimensions of the breast shown and the extent of the probe array are compatible. It should be understood that during the placement of the probe, real time images (acquired about once every 50-80 msec) of the capacitance and the conductance are shown, for example in the large squares to the left of the display.

Fig. 14, which represents an actual imaging situation shows, in the leftmost of the small images, a situation in which a small atypical hyperplasia which was previously detected by other means. This position shows an elevated conductivity and a very slightly reduced capacitance. In position 2, which is also shown in the two large squares to the right of the display, a previously unsuspected area having a capacitance/conductance profile characteristic of atypical hyperplasia is detected.

Fig. 15 shows a study typical of multiple suspected sites of carcinoma (in positions 2 and 4). The images of position 4 are shown in enlarged format at the left of the

image. In these sites, both the capacitance and conductance are elevated with respect to their surroundings.

Alternatively, a composite image such as the image of the sum of the capacitance and conductance images, their product, their sum or their ratio can be displayed to give a similar indication of the type of detected anomaly. A color coded composite image can also be displayed, where, for example, the median value for each image would be black and where positive and negative values would have a particular color which, when combined would result in distinctive colors for suspect impedance deviations.

The display shown in Figs. 14 and 15 can also be utilized to show a plurality of images of the same region at varying frequencies and one or more different impedance measures of a given region.

Figs. 17A and 17B show a block diagram of a preferred embodiment of a system 200 which incorporates a number of multi-element probes. It should be understood that the exact design of system for impedance imaging will depend on the types of probes attached to the system and the exact imaging modalities (as described above) which are used.

As shown in Figs. 17A and 17B the preferred system can incorporate biopsy needle probe 154, two plate probes 28, 30 such as those shown in Figs. 1-3, scan zoom probe 100 such as that shown in Fig. 6A, conformal probe 139 such as that shown in Fig. 7B, a bra-cup probe, finger/glove probe 130 such as that shown in Fig. 7A, laparoscopic probe 150 such as that shown in Fig. 9 or an intra-operative probe 140 as shown in Fig. 8. Furthermore, when three probes are used as in Fig. 11E, provision is made for attachment of a third plate probe. The position of the plate and needle probes is controlled by controller 181 as described in respect to Fig. 11D.

The probes as connected via a series of connectors, indicated by reference numeral 302 to a selection switch 304 which chooses one or more of the probes in response to a

command from a DSP processor 306. Selection switch 304 switches the outputs of the probes, namely the signals detected at the sensing elements of the probes (or amplified versions of these signals) to a set of 64 amplifiers 308, one amplifier being provided for each sensing element. For those probes, such as the large plate probes, which have more than 64 sensing elements, the selection switch will (1) sequentially switch groups of 64 sensing elements to amplifier set 308, (2) choose a subset of sensing elements on a coarser grid than the actual array by skipping some elements, as for example every second element, (3) sum signals from adjacent elements to give a new element array of lower resolution and/or (4) choose only a portion of the probe for measurement or viewing. All of these switching activities and decisions are communicated to the switch by DSP processor 306 which acts on command from a CPU 312. The output of the amplifiers is passed to a multiplexer 307 where the signals are serialized prior to conversion to digital form by a, preferably 12-bit, A/D convertor 310. A programmable gain amplifier 309, preferably providing a gain which is dependent on the amplitude of the signals, is optionally provided to match the signal to the range of the A/D convertor. The output of A/D 310 is sent to the DSP for processing as described above. In a preferred embodiment of the invention DSP 306 is based on a Motorola MC 68332 microprocessor.

While 64 amplifiers has been chosen for convenience and lower cost, any number of amplifiers can be used.

The DSP calculates the impedance results and send the results to CPU 312 for display on a graphic data display 16, printing on a printer 18 or other output signals generation as described above by a light indicator 314 or a sound indicator 316.

Alternatively, the DSP directs signal sampling and averages together the samples or pre-processes them, sending the averaged or pre-processed samples to CPU 312, which then

performs the impedance calculations.

The CPU may also receive images from video camera 256, for example, when used with an intra-operative probe, from an endoscopic optics and camera system 320, for example when the camera views the outer surface of the laparoscopic probe or from an ultra sound imager 322, for example, in biopsy performance as shown in Figs. 11A and 11B. When an image is acquired from one of these cameras a frame grabber 324 is preferably provided for buffering the camera from the CPU. As described above, the CPU combines these images with the impedance images provided by one or more probes for display or other indication to the operator.

Fig. 15 also shows a programmable reference signal generator 326 which receives control and timing signals from the DSP. The reference signal generator generates excitation signals which are generally supplied, during impedance imaging, to reference probe 13, which, as described above, is placed at a point (or at more than one point) on the body remote from the region of impedance measurement. Signal generator 312 may produce a sinusoidal waveform, pulses or spikes of various shapes (including a bipolar square shape) or complex polychromatic waveforms combining desired excitation frequencies. Appropriate impedance calculations, in DSP 306 or in CPU 312, are implemented in accordance with the waveform of the excitation.

Where a breast is imaged and one of the two plates is used as the source of excitation, as described above, the output of signal generator is sent to the exciting plate (signal paths not shown for simplicity). A current overload sensor 330 is preferably provided after the signal generator to avoid overloads caused by short circuits between the reference probe and the imaging probe or ground.

Also shown on Fig. 17A is an internal calibration reference 332 which is preferably used for internal calibration of the system and for testing and calibration of the probes.

For internal testing and calibration, calibration reference 232 receives the signals generated by the programmable reference signals generator as passed to the selection switch, in series with an internal admittance in the calibration reference, as selected by the DSP processor. The DSP processor computes the admittance from signals received from the A/D convertor and compares the computed admittance with the actual admittance provided by internal calibration reference 332. This comparison can be provide an indication that the system requires adjustment or repair or can be used to calibrate the system.

Similarly, the output of calibration reference 332 may be provided to probe cover 88 for calibration and quality assurance of a plate or scan probe as described above. Under this situation, the DSP instructs selection switch 304 to choose the input from the respective probe.

Also provided is a user interface 334 such as a keyboard, mouse, joystick or combinations thereof, to allow the operator to enter positional information via the screen and to choose from among the probes provided and from the many options of calculation, display, etc.

Although described together as the preferred embodiment of the invention, it is not necessary to use the probes of the invention, the methods of calculation of impedance and impedance characteristics of the invention and the preferred apparatus of the invention together. While it is presently preferred that they be used together they may each be used with probes, calculation methods and apparatus for impedance imaging as applicable and as available.

Certain aspects of the invention have been described with respect to a biopsy needle or with respect to placement of such a needle. It should be understood that such description and aspects of the invention are equally applicable to positioning needles, catheters, endoscopes, etc.

Although various embodiments, forms and modifications

have been shown, described and illustrated above in some detail in accordance with the invention, it will be understood that the descriptions and illustrations are by way of example, and that the invention is not limited thereto but encompasses all variations, combinations and alternatives falling within the scope of the claims which follow:

CLAIMS

1. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface;

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements; and

a partition separating the individual sensing elements such that when the individual probes contact the tissue surface they are substantially electrically isolated from each other.

2. A probe according to claim 1 wherein the sensing elements comprise a conductive, viscous gel.

3. A probe according to claim 1 wherein the sensing elements comprise a conductive, flexible, solid.

4. A probe according to claim 1 wherein the sensing elements comprise a sponge impregnated with a conductive viscous gel.

5. A probe according to claim 1 wherein each individual sensing element is located in a well formed by the partition and a substrate underlying the sensing element.

6. A probe according to claim 5 wherein the side of the substrate opposite the sensing elements is formed with an alignment structure for aligning the multi-element probe.

7. A probe according to claim 5 wherein the well is formed by embossing the partition on a sheet of material, whereby the un-embossed portion of the sheet forms the substrate underlying the sensing element.

8. A probe according to claim 6 wherein the well is formed by embossing the partition on a sheet of material, whereby the un-embossed portion of the sheet forms the substrate underlying the sensing element and wherein the indentations are the back of the embossed wells.

9. A probe according to claim 5 wherein the well is formed by laminating a grid formed by holes punched in a sheet or formed by extrusion to the substrate.

10. A probe according to claim 5 wherein the well is formed by printing the partitions onto the substrate.

11. A probe according to claim 5, including an electrical connection between a first surface of the substrate inside the well and a second, opposite, surface of the substrate.

12. A probe according to claim 11 and also comprising an anisotropic conductive sheet overlying the second surface of the substrate.

13. A probe according to claim 11 and also comprising a conductive contact on the second surface of the substrate which is electrically connected to the first surface of the substrate and an adhesive contact overlying the conductive contact.

14. A probe according to claim 1 wherein the sensing elements do not extend past the top of the partition.

15. A probe according to claim 14 wherein the sensing elements do not extend to the top of the partition.

16. A probe according to any of the preceding claims and including a cover having a conductive surface facing the front portion of the sensing elements.

17. A multi-element probe for providing an electrical connection to tissue comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue;

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements; and

a cover having a surface facing the front portion of the sensing elements, at least that portion of said surface facing the sensing elements being an electrically conductive surface.

18. A multi-element probe according to claim 17 wherein said cover is formed of a flexible material and wherein, in an unstressed position said electrical conductive surface does not contact said conductive sensing elements.

19. A multi-element probe according to claim 18 wherein said cover is so configured that the surface contacts the sensing elements when a surface of the cover opposite the conductive surface is pressed toward the sensing elements.

20. A multi-element probe according to claim 17 wherein the cover also includes an area, on the surface facing the individual sensing elements, remote from the individual sensing elements, which is a conductive area electrically connected to said portions facing the sensing elements, the multi-element probe also including a contact electrically connected to the exterior of the probe.

21. A multi-element probe according to claim 20 wherein, in an unstressed position, said electrical conductive surface does not contact said contact and wherein said cover is so configured that the conductive area contacts the contact

when a surface of the cover opposite the conductive surface is pressed toward the sensing elements.

22. A multi-element probe according to claim 17 and further comprising at least one contact suitable for connection to an external source of electrical energy and also including impedance elements between the conductive surfaces opposite the sensing elements and the contact.

23. A multi-element probe according to claim 20 and also including impedance elements between the conductive surfaces opposite the sensing elements and the contact.

24. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the side of the substrate opposite the sensing elements is formed with indentations for aligning the multi-element probe.

25. A multi-element probe for the measurement of impedance of tissue, wherein the elements of the probe are sufficiently transparent to allow visualization of tissues beneath the probe when the probe is placed in contact with the tissues.

26. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements, wherein

the probe is sufficiently transparent to allow visualization of tissues beneath the probe when the probe is placed in contact with the tissues.

27. A multi-element probe according to any of claims 1-16 or 17-26, wherein the sensing elements are formed of a spongy conductive material.

28. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the sensing elements are formed of a spongy conductive material.

29. A multi-element probe according to any of claims 1-16, 17-26 or 28 wherein the sensing elements are formed on a flexible surface, whereby the multi-element probe conforms, at least in part, to the tissue.

30. A multi-element probe according to any of claims 1-16, 17-26 or 28, wherein the probe is provided with apertures between sensing elements suitable for the passage of a thin elongate object.

31. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the

tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the probe is provided with apertures between sensing elements suitable for the passage of a thin elongate object.

32. A multi-element probe for providing an electrical connection to a tissue surface comprising:

an array of individual conductive sensing elements spaced over a surface, each element having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein the area of the conductive elements comprises less than 70% of the total area encompassed by the array.

33. A multi-element probe according to any of claims 1-16, 17-26, 28, 31 or 32, wherein at least a portion of the surface of the probe facing the tissue to be measured is adhesive to the tissue.

34. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a plurality of conductive elements providing an electrical connection to the respective individual sensing elements,

wherein at least a portion of the surface of the probe facing the tissue to be measured is adhesive to the tissue.

35. A multi-element probe according to any of claims 1-16,

17-26, 28, 31, 32 or 34, and including:

means for attaching the probe to the finger of a person whereby the person can perform palpative examination concurrently with impedance imaging.

36. A multi-element probe for providing an electrical connection to a tissue surface comprising:

a plurality of individual conductive sensing elements, each having a front portion suitable for contact with the tissue surface; and

a glove having fingers, said sensing elements being attached to the outside of one of the glove at one of the fingers whereby a wearer of the glove can perform palpative examination concurrently with impedance imaging.

37. A multi-element intermediate device for providing an electrical connection between a multiconductor sensor device and a tissue surface comprising a plurality of individual conductive sensing elements, substantially electrically insulated from each other, each having a front portion suitable for contact with the tissue surface and a back portion detachably matable to the multi-conductor sensor device.

38. An intermediate device according to claim 37 and including electrical contacts on the back portion which are electrically connected to the sensing element and which contact a plurality of mating contacts on the multi-conductor sensor device.

39. A multi-element intermediate device for providing an electrical connection between a multiconductor sensor device and a tissue surface comprising:

a multi-element probe according to any of claims 1-15, 17-26, 28, 31, 32 or 34, and having a back portion detachably matable to the multi-conductor sensor device.

40. An intermediate device according to claim 39 and including electrical contacts on the back portion which are electrically connected to the sensing element and which contact a plurality of mating contacts on the multi-conductor sensor device.

41. A catheter or endoscopic probe comprising:

a multi-element probe according to any of claims 1-16, 17-26 or 28; and

a fiber optic viewer whose field of view includes at least one surface of the probe when the probe is in contact with the tissue.

42. A catheter or endoscopic probe comprising:

a multi-element probe for providing an electrical connection to a tissue surface, the probe including a plurality of individual conductive sensing elements on a substrate, each sensing element having a front portion suitable for contact with the tissue surface and fiduciary marks visible from an other surface; and

a fiber optic viewer whose field of view includes at least the other surface of the probe.

43. Apparatus for impedance imaging of a breast comprising:

a multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

an electrode adapted for mounting on a side of the breast substantially opposite the multi-element probe; and

a source of electrical energy which provides a voltage between at least a portion of the electrode and at least one element of the probe.

44. Apparatus for impedance imaging of a breast comprising:

a multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

an electrode adapted for mounting on a side of the

breast substantially opposite the multi-element probe;

an additional electrode adapted for mounting on portion of the body remote from the breast; and

a source of electrical energy which provides a voltage between the additional electrode and at least one element of the probe.

45. Apparatus according to claim 43 or claim 44 wherein the multi-element probe and the electrode adapted for mounting on a side of the breast form respective parallel planes.

46. Apparatus according to claim 43 or claim 44 wherein the multi-element probe and the electrode adapted for mounting on a side of the breast form two planes at an angle to each other.

47. Apparatus according to claim 43 or claim 44 and including a plurality of receivers which measure an electrical signal at the sensing elements.

48. Apparatus according to claim 43 or claim 44 wherein the electrode adapted for mounting on a side of the breast comprises a second multi-element probe.

49. Apparatus according to claim 43 wherein the multi-element probe comprises a multi-element probe according to any of claims 1-16, 17-26, 28, 31, 32 or 34.

50. Apparatus according to claim 49 wherein at least one of the multi-element probes is rigid and non-planar in accordance with the shape of a body structure.

51. Apparatus according to claim 49 wherein at least one of the multi-element probes is flexible so as to conform to the shape of a body structure.

52. Apparatus for impedance imaging of a breast comprising:

a first multi-element probe comprising a plurality of sensing elements and adapted for mounting on one side of a breast;

a second multi-element probe adapted for mounting on a side of the breast substantially opposite the multi-element probe; and

a source of electrical energy which alternatively energizes at least some of the elements of one or the other of the first and second multi-element probes by supplying a voltage thereto, wherein the unenergized one of the multi-element probes forms an image based on the voltage applied to the energized probe.

53. Apparatus according to claim 52 wherein the first and second multi-element probes form respective parallel planes.

54. Apparatus according to claim 52 wherein the first and second multi-element probes form two planes at an angle to each other.

55. Apparatus according to any of claims 52-54 and including a plurality of receivers which measure an electrical signal at the sensing elements.

56. Apparatus according to claim 52 wherein the multi-element probe comprises a multi-element probe according to any of claims 1-16, 17-26, 28, 31, 32 or 34.

57. Apparatus for impedance imaging of tissue comprising:

an impedance probe which produces signals representative of impedance values below the elements and having fiduciary marks which are visible when the probe contacts the tissue;

an impedance image generator which receives the signals and produces an impedance image;

a video camera which views the probe and tissue and generates a video image; and

a video image processor which receives a video image of the tissue without the probe in place and an image of the tissue with the probe in place, and provides a video image of the tissue with the fiduciary marks and impedance image superimposed thereon.

58. A method of impedance imaging of a region of the body comprising:

(a) positioning a multi-element probe, comprising a plurality of sensing elements, on one side of the region;

(b) positioning an electrode on a side of the region substantially opposite the multi-element probe;

(c) electrifying the electrode; and

(d) measuring a signal at at least some of the elements of the multi-element probe.

59. A method of impedance imaging of a region of the body comprising:

(a) positioning a multi-element probe, comprising a plurality of sensing elements, on one side of the region;

(b) positioning an electrode on a side of the region substantially opposite the multi-element probe;

(c) positioning a second electrode on a portion of the body;

(d) electrifying the second electrode; and

(e) measuring a signal at at least some of the elements of the multi-element probe.

60. A method according to claim 58 or claim 59 wherein (b) comprises positioning a second multi-element probe on a side of the region substantially opposite the multi-element probe.

61. A method of impedance imaging of a region of the body

comprising:

positioning a first multi-element probe, comprising a plurality of sensing elements, on one side of the region;

positioning a second multi-element probe on a side of the region substantially opposite the multi-element probe;

electrifying fewer than all of the plurality of sensing elements of the second multi-element probe; and

measuring a signal at at least some of the elements of the first multi-element probe.

62. A method of impedance imaging of a region of the body comprising:

contacting one side of the region with a first multi-element probe, comprising a first plurality of sensing elements;

contacting a second side of the region with a second multi-element probe, comprising a second plurality of sensing elements;

receiving signals from said first and second multi-element probes in response to a stimulus; and

combining the signals received from both probes to locate objects within the region.

63. A method for guidance in the placement of an elongate element in a region of a subject comprising:

(a) inserting the elongate element into tissue, said element including a plurality of impedance measuring sensing element thereon;

(b) measuring the impedance between the plurality of sensing elements and an electrode in contact with the subject; and

(c) guiding the element to a desired position having defined impedance properties in response to measurements of impedance made in (b).

64. A method according to claim 63 and also including;

imaging the region of the subject including the elongate element and generating an image thereof;

receiving the image and the measurements of impedance made in (b) and superimposing a representation of the impedance measurements on the image of the elongate element and surrounding tissues; and

displaying said superimposed images.

65. A method according to claim 64 wherein the outer surface of the elongate element is formed with a matrix of impedance measuring elements each measuring the tissue impedance in a direction generally perpendicular to the element and wherein the display indicates a guiding direction for the elongate element based on the impedance measurements.

66. A method according to any of claims 63-65 wherein the elongate element is inserted into the body through a hole in an array of impedance probe elements and including:

providing a two-dimensional impedance image based on signals received by the array;

guiding the elongate element based on the two-dimensional image; and

determining the desired depth of the elongate element based on impedance signals received from the impedance measuring elements on the elongate element.

67. A method for guidance in the placement of an elongate element in portion of a patient comprising:

forming a first two-dimensional impedance image of at least a part of said portion from a given direction;

forming a second two dimensional impedance image of at least a part of the portion using a multi-element impedance probe placed at a known angle to the plane of the first image;

inserting the elongate element between elements of the

multi-element probe; and

guiding the elongate element to a point of impedance deviation at least partially under the guidance of the first and second two dimensional images.

68. A method comprising:

providing an impedance measurement system including a multi-element probe attached to at least one finger of an examiner; and

providing an indication of impedance generated on the basis of signals detected by said elements, whereby both a tactile and impedance indication of an examined tissue are simultaneously acquired.

69. A method for improving the sensitivity of impedance imaging comprising:

contacting tissue with a multi-element probe;

contacting a different portion of tissue with at least one electrode;

exciting the at least one electrode with a pulsed voltage;

measuring signals, responsive to said pulsed voltage at at least a plurality of the elements of the probe;

computing the real and imaginary parts of an admittance represented by said voltage and signals for a plurality of frequencies at a plurality of said elements; and

choosing at least one frequency as a measurement frequency which gives a large difference for said measures at different elements of the probe.

70. A method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

manipulating the tissue underlying the probe while the probe remains in stationary contact with the surface of the

tissue; and

identifying as a non-artifact those impedance deviations which shift in the direction of the manipulation on the impedance map.

71. A method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

moving the probe along the surface of the tissue; and

identifying as an artifact those impedance deviations which remain stationary or disappear in the impedance map as the probe is moved.

72. A method for identifying, in a multi-element impedance probe which forms an impedance map of tissue when placed on the surface thereof, artifacts among impedance deviations from the surroundings, the method comprising:

moving the probe together with the tissue; and

identifying as a fixed artifact those impedance deviations which move on the impedance map, in the opposite direction from the movement of the probe and the tissue.

73. A method of displaying impedance imaging information comprising:

displaying at least one impedance image of a region; and

displaying an indication of the imaged region on a representation of the physiology of the patient.

74. A method of displaying according to claim 73 and including:

simultaneously displaying both a capacitance and a conductance map of the same region.

75. A method of displaying impedance imaging information

comprising:

displaying a capacitance map of a region; and

simultaneously displaying a conductance map of the same region.

76. A method of displaying impedance imaging information comprising:

computing maps of a plurality of imaging measures; and

simultaneously displaying the measures.

77. A method of displaying impedance information comprising:

computing a plurality of maps of at least one imaging measure at a plurality of frequencies; and

simultaneously displaying the maps.

78. A method of identifying a suspected carcinoma comprising:

comparing a capacitance map of a region to a conductance map of the same region;

identifying a deviation from the surroundings as a suspected cancer if at some frequency less than about 10 kHz both the capacitance value and the conductance value are higher than that of the surroundings.

79. A method of identifying a suspected atypical hyperplasia comprising:

comparing a capacitance map of a region to a conductance map of the same region;

identifying a deviation from the surroundings as a suspected cancer if at some frequency less than 10 kHz both the capacitance value and the conductance value are higher than that of the surroundings.

80. A method of differentiating a suspected carcinoma from a suspected atypical hyperplasia comprising:

comparing a capacitance map of a region to a conductance map of the same region;

classifying a deviation from the surroundings as a suspected atypical hyperplasia if at some frequency less than 10 kHz the capacitance value is lower than that of the surroundings and the conductance value is higher than that of the surroundings; and

classifying a deviation from the surroundings as a suspected cancer if at some frequency less than 10 kHz both the capacitance value and the conductance value are higher than that of the surroundings.

81. A method according to any of claims 78 to 80 wherein the frequency at which the comparison of the capacitance and conductance values take place is below 2500 Hz.

82. A method according to any of claims 78 to 80 wherein the frequency at which the comparison of the capacitance and conductance values take place is below 500 Hz.

FIG. 1

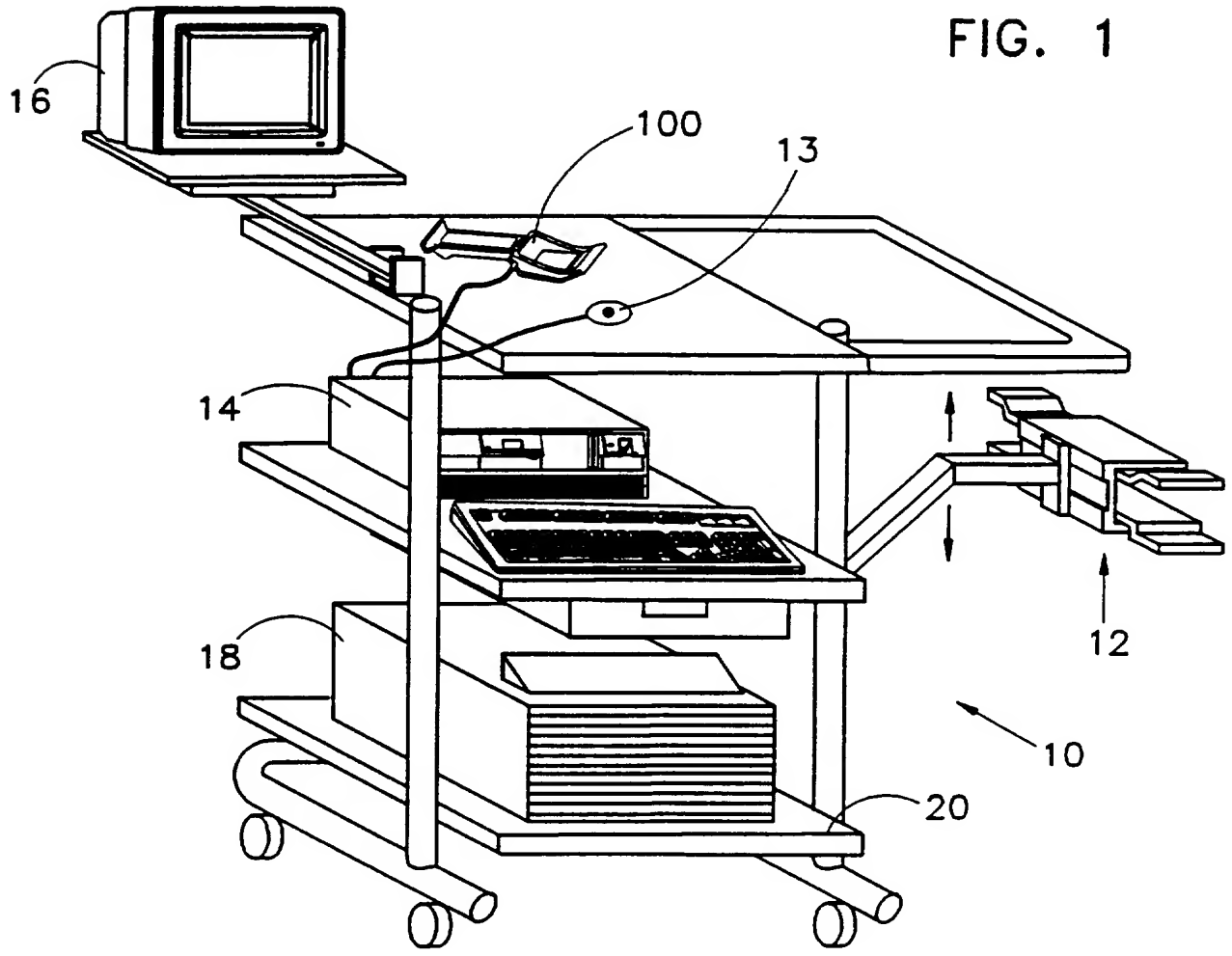


FIG. 2

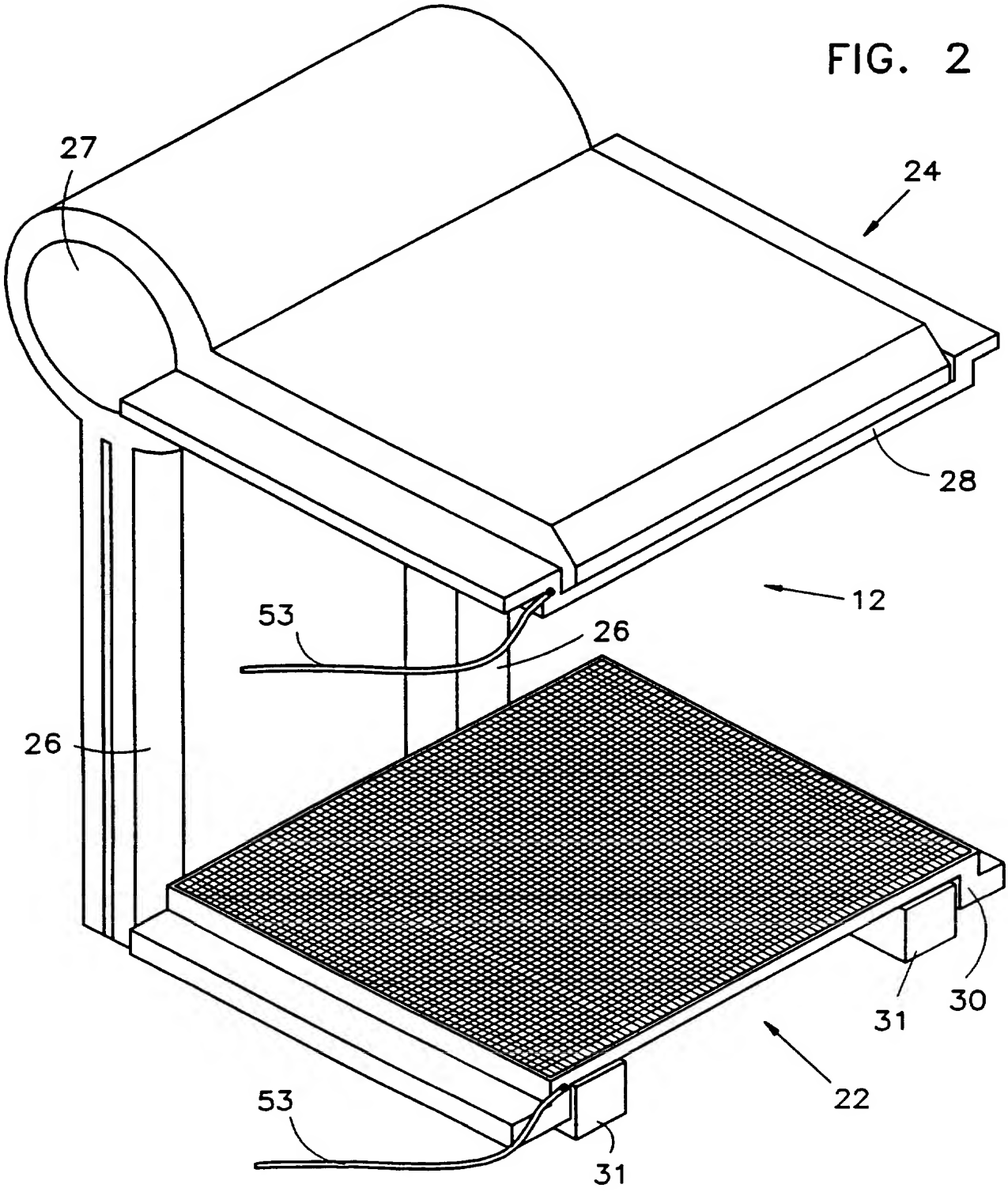


FIG. 3A

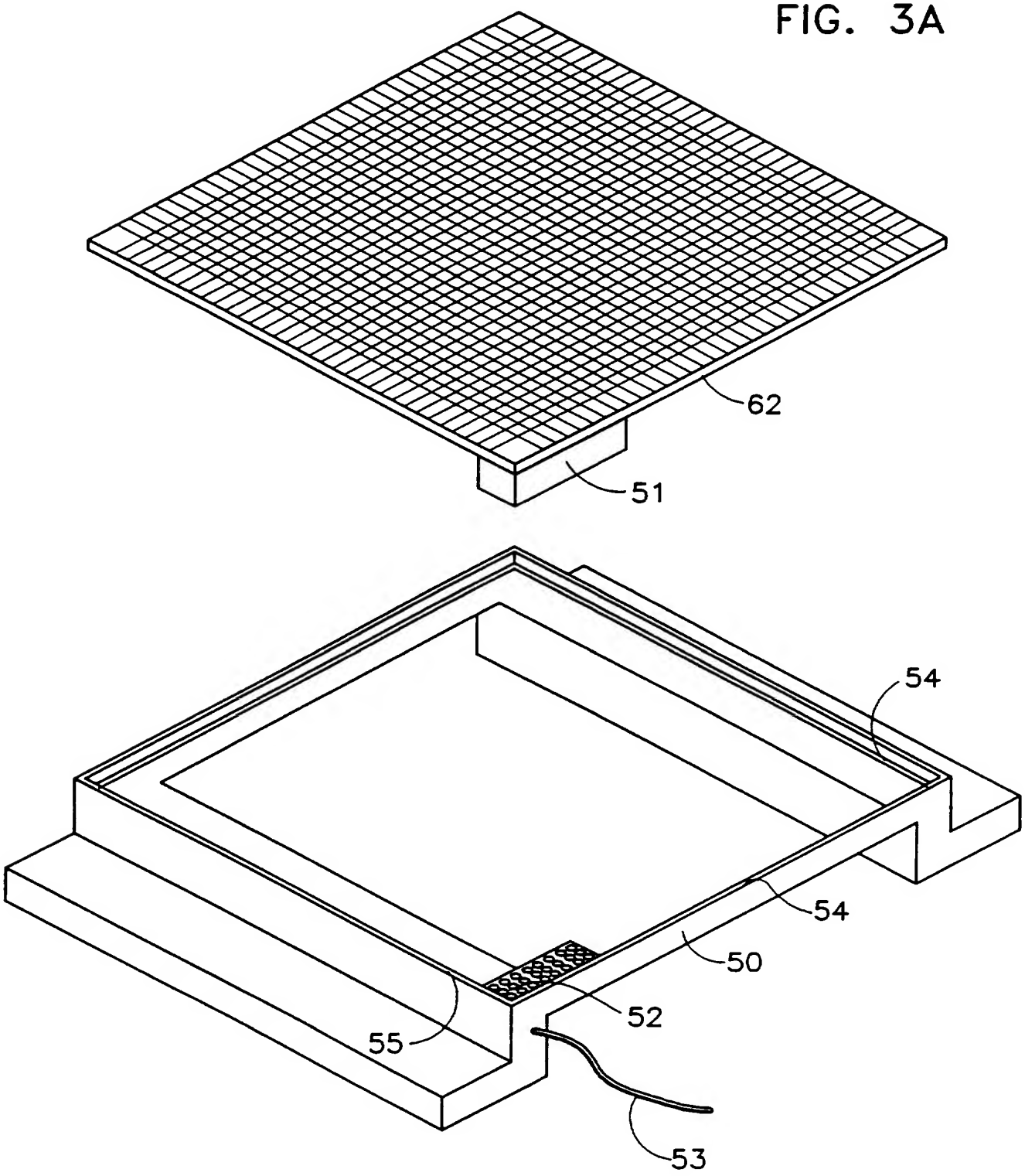


FIG. 3B

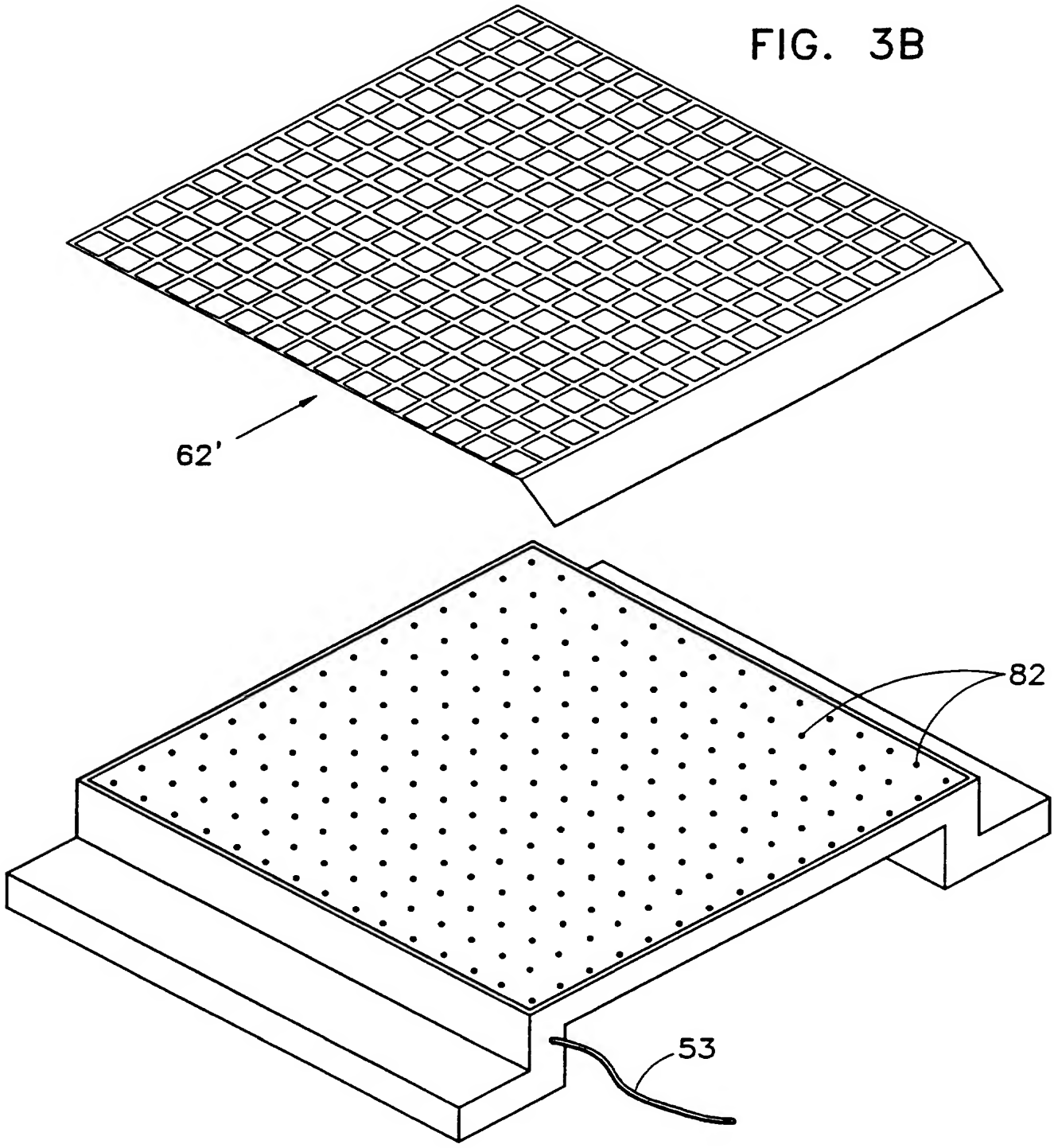


FIG. 4

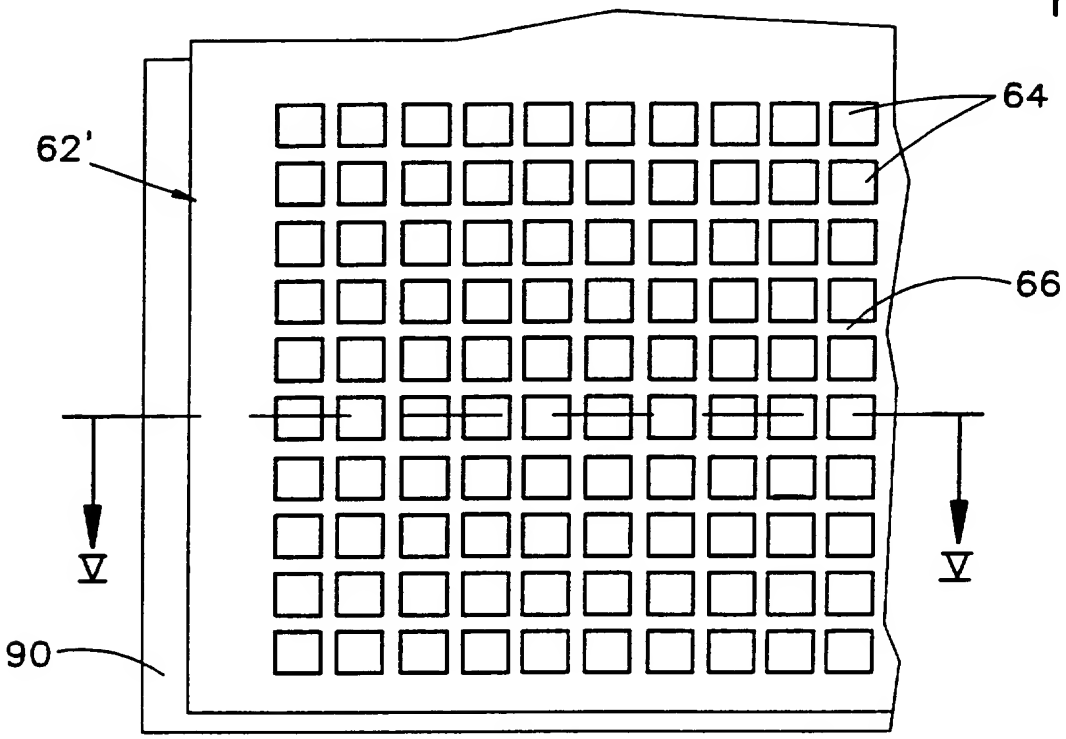
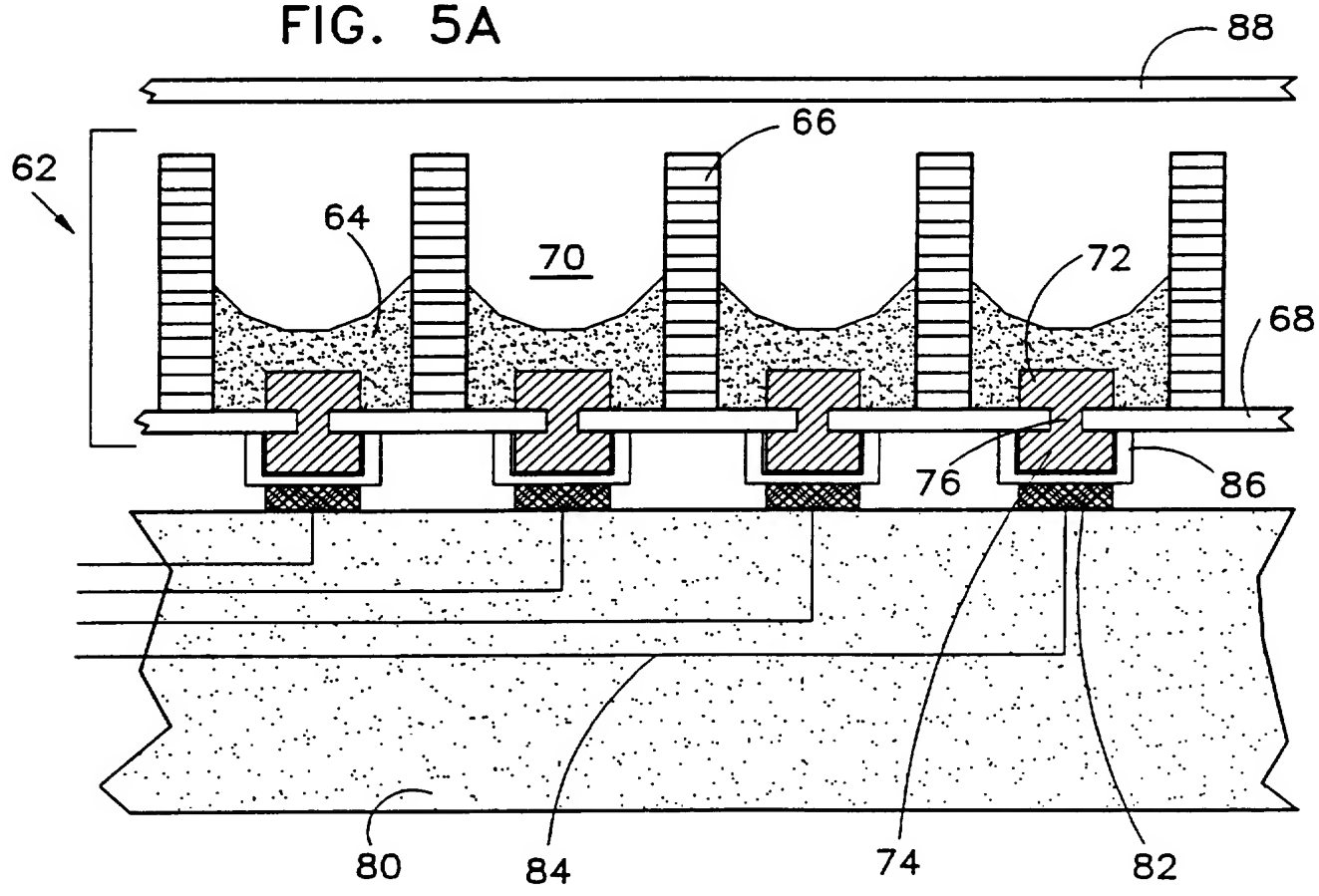
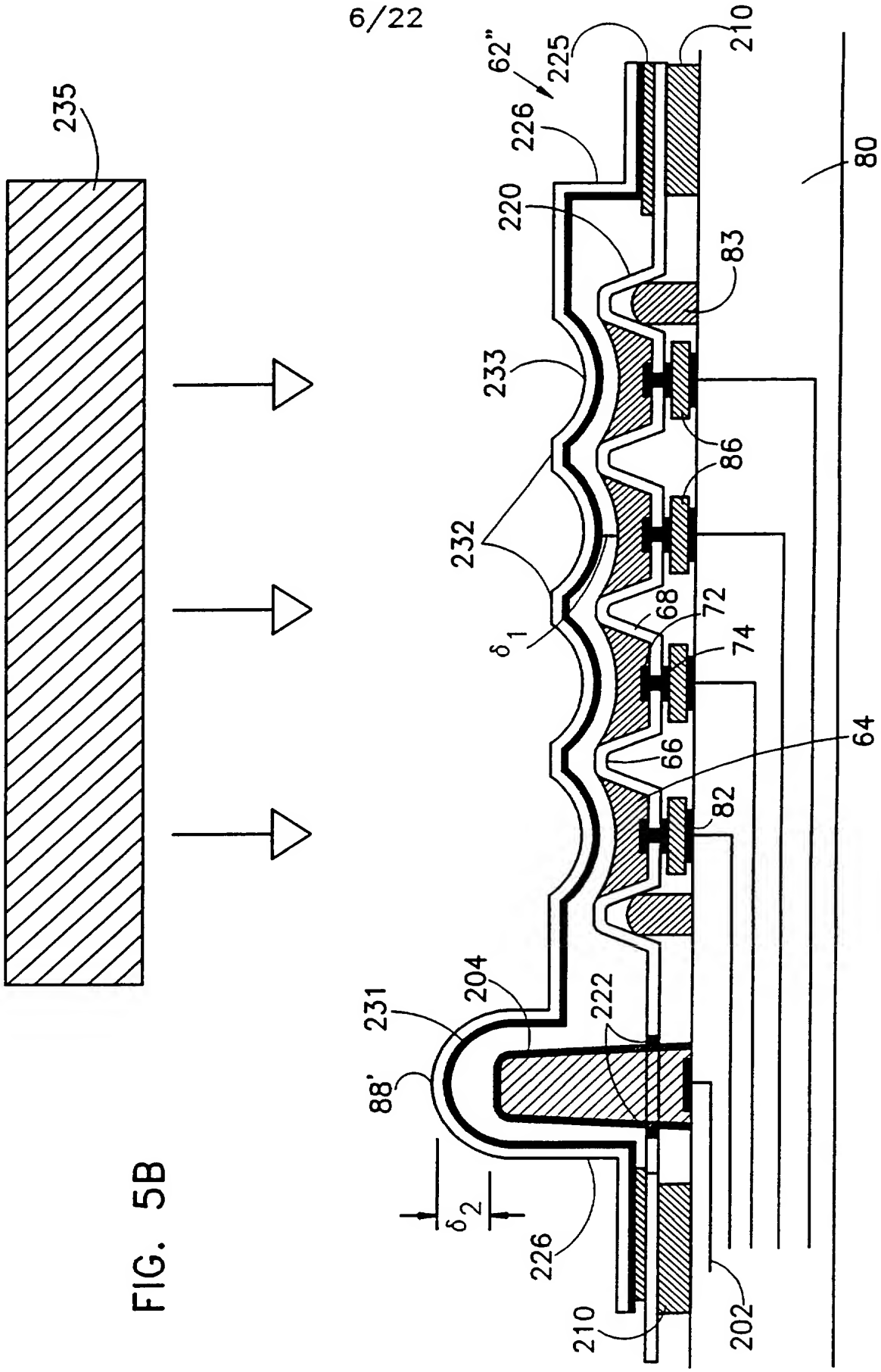


FIG. 5A

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226
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220
83
233
86
232
68
72
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δ_1
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66
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231
204
222
88'
δ_2
226
210
202

FIG. 5B

FIG. 5C

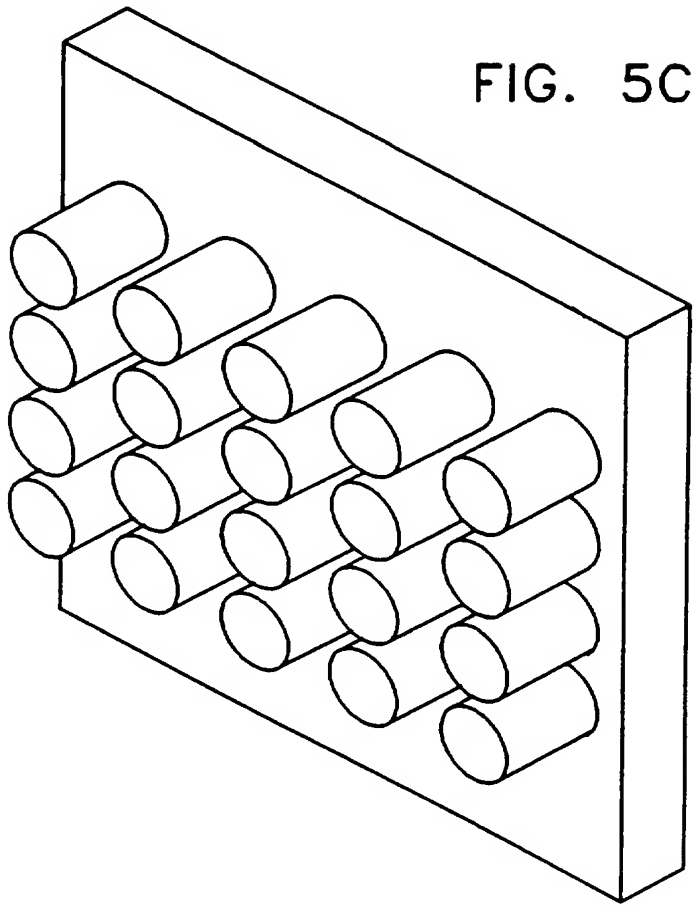


FIG. 6A

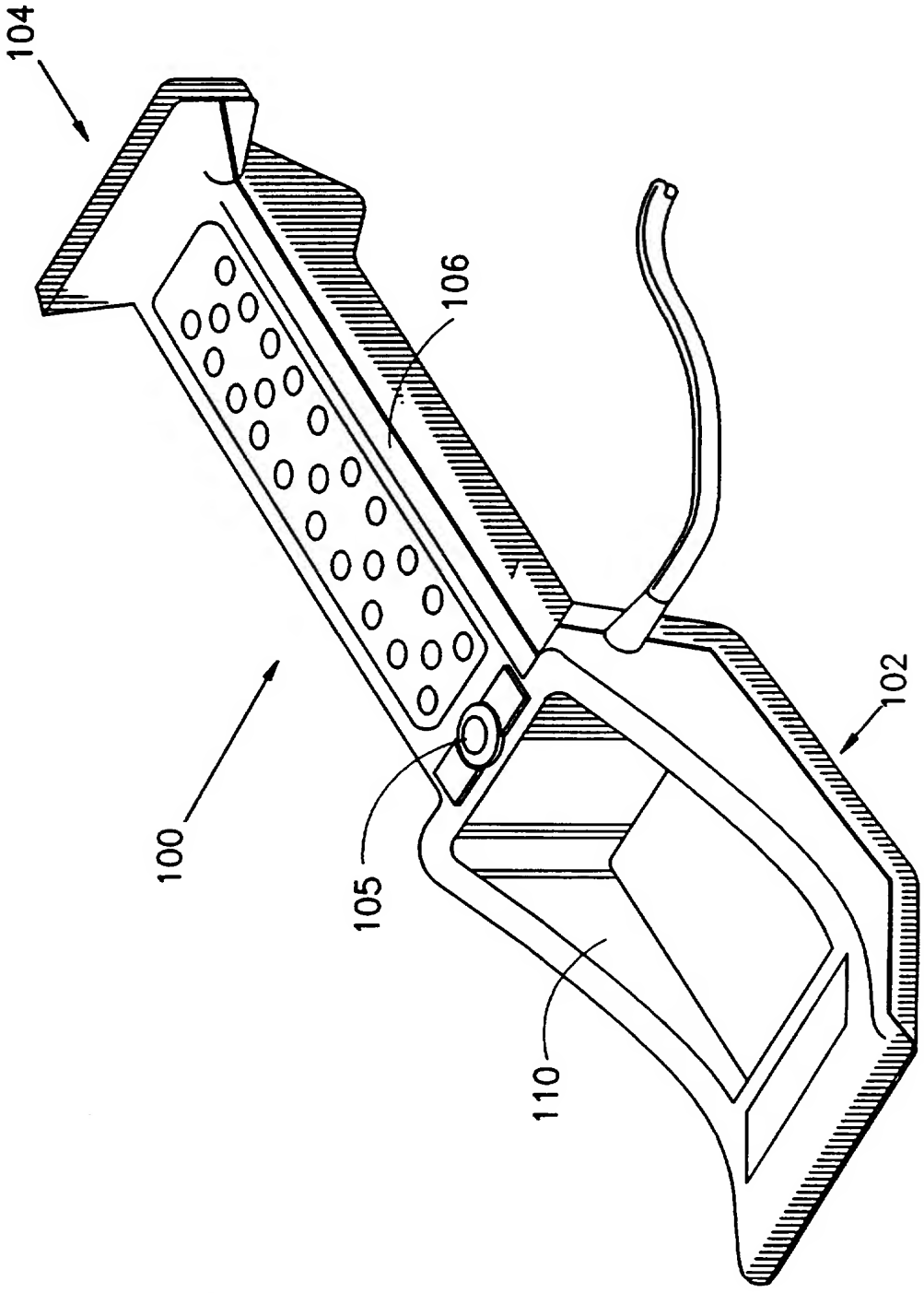


FIG. 6B

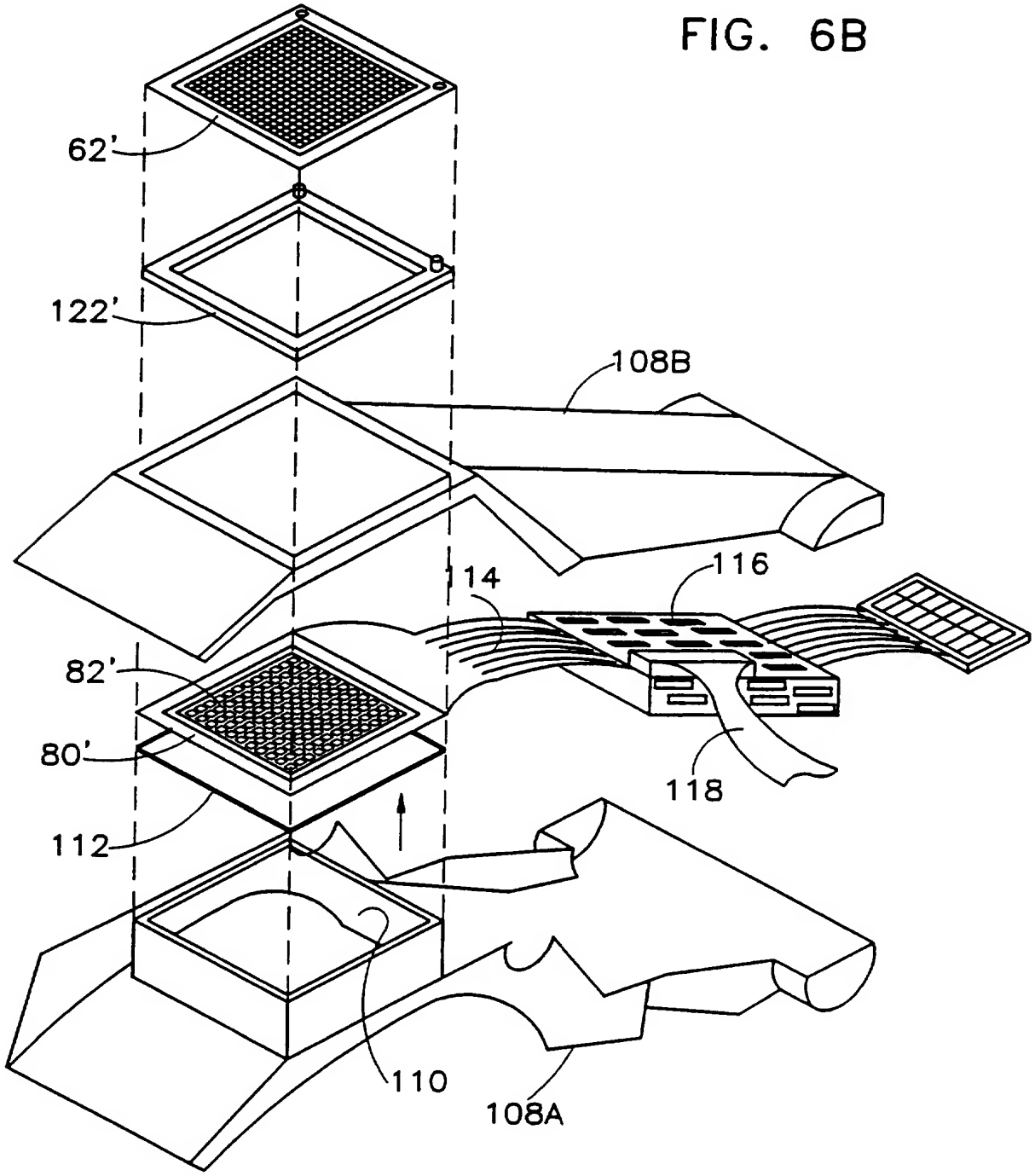


FIG. 7A

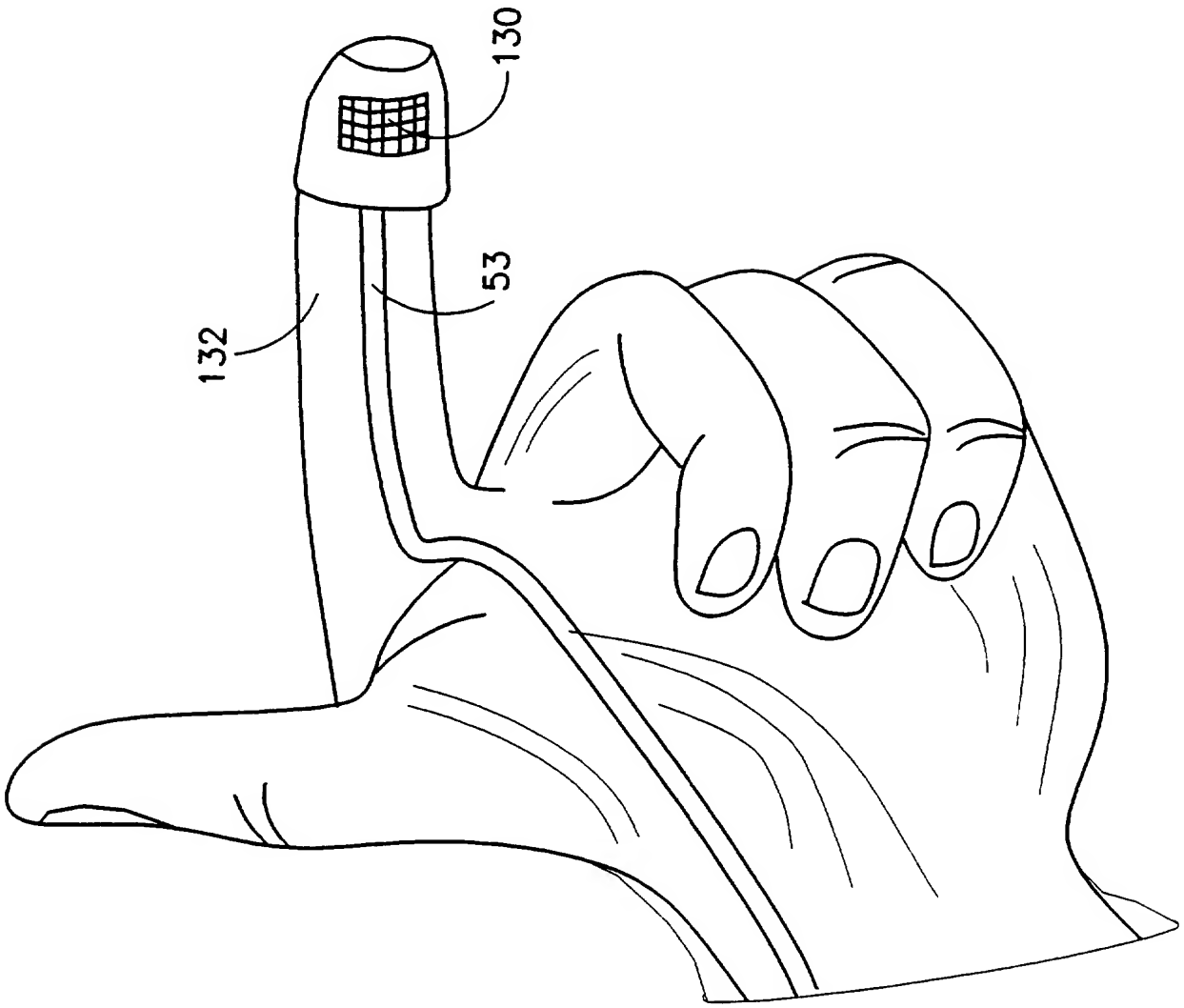


FIG. 7B

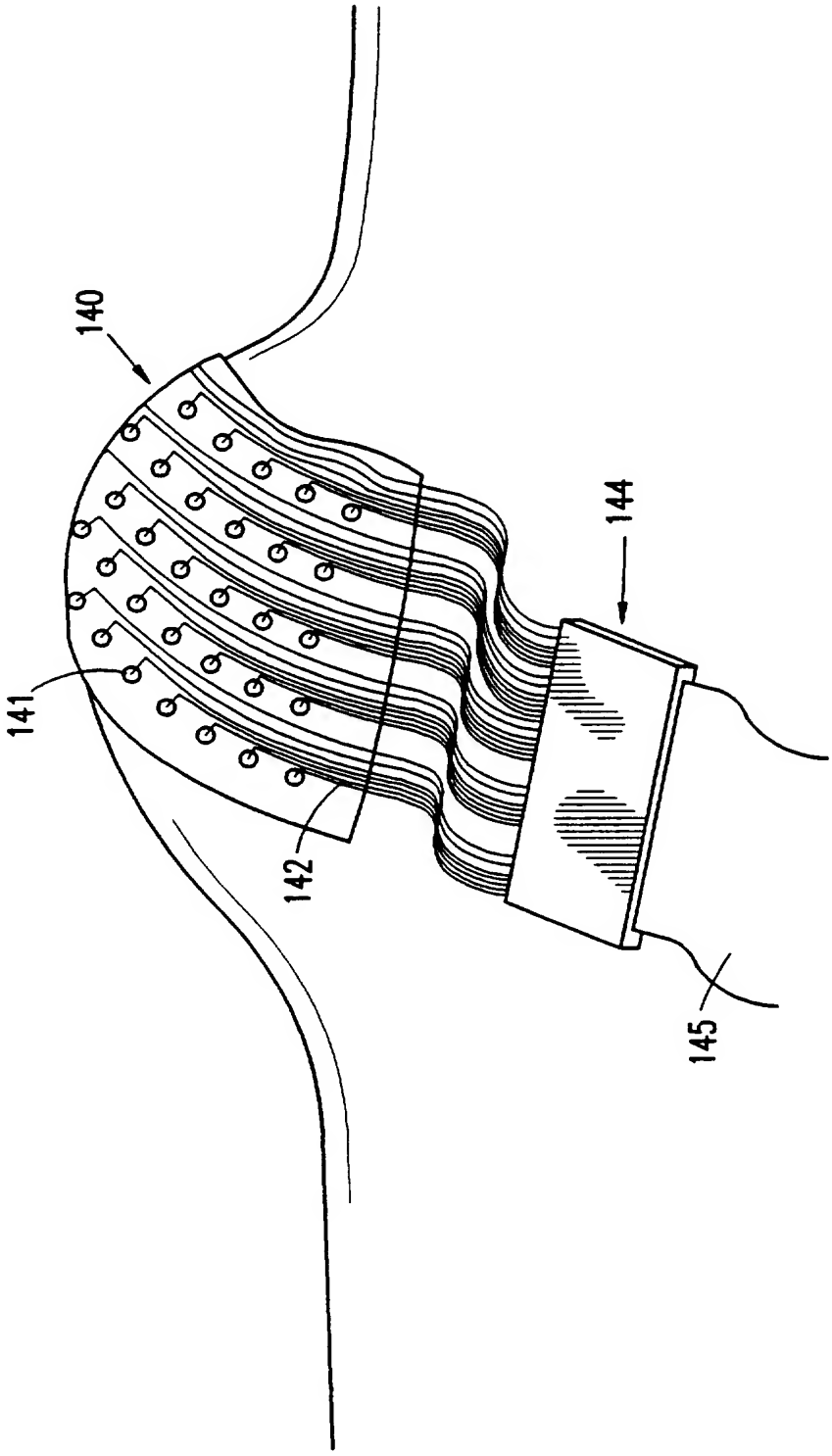


FIG. 10

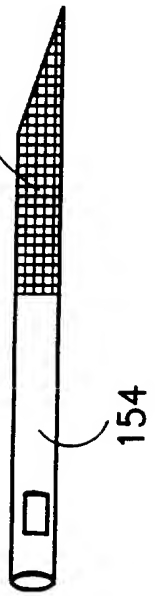


FIG. 9

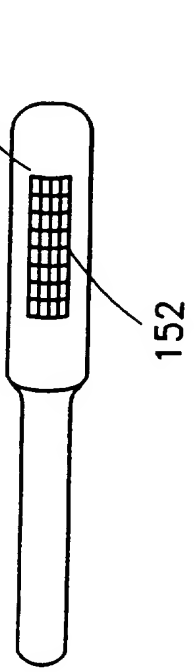


FIG. 8

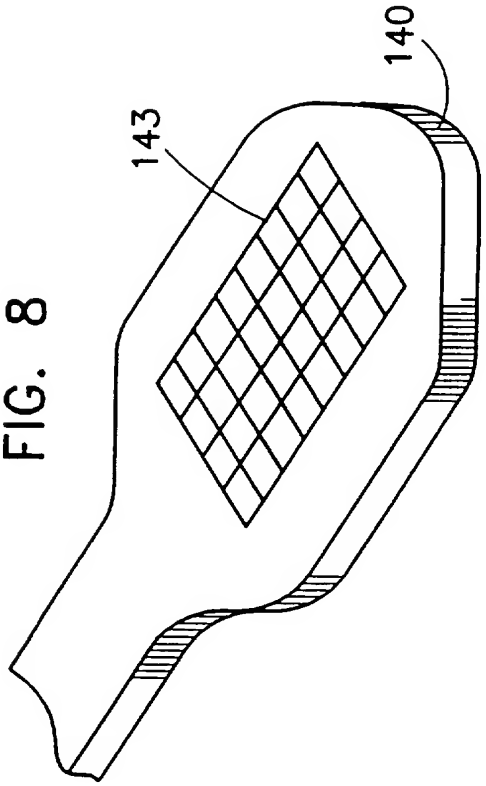


FIG. 11A

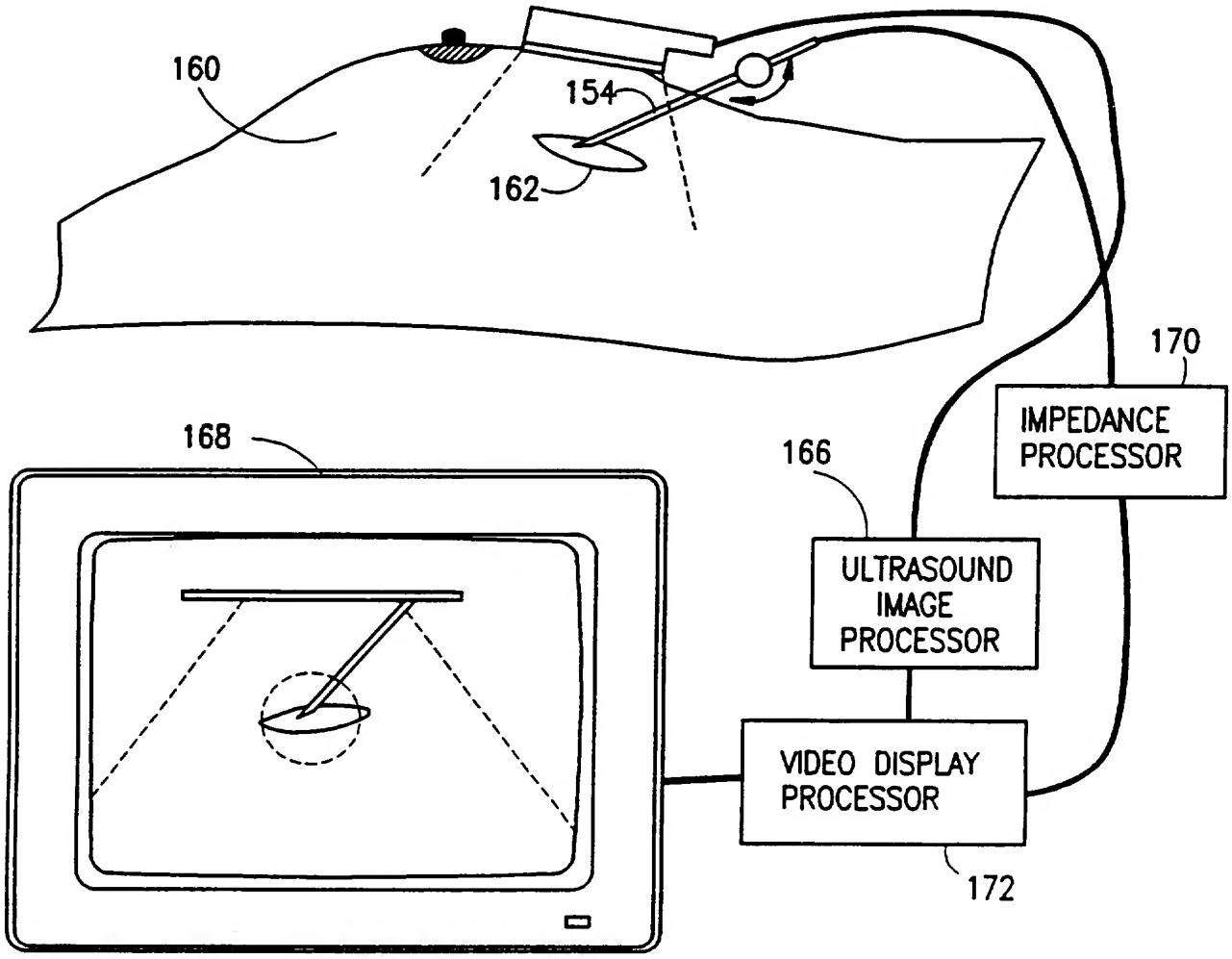
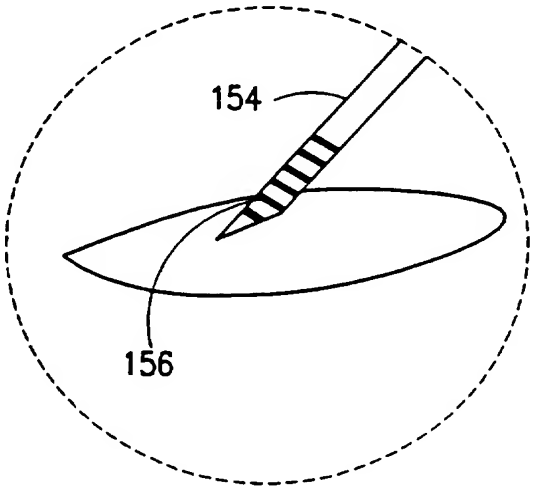


FIG. 11B



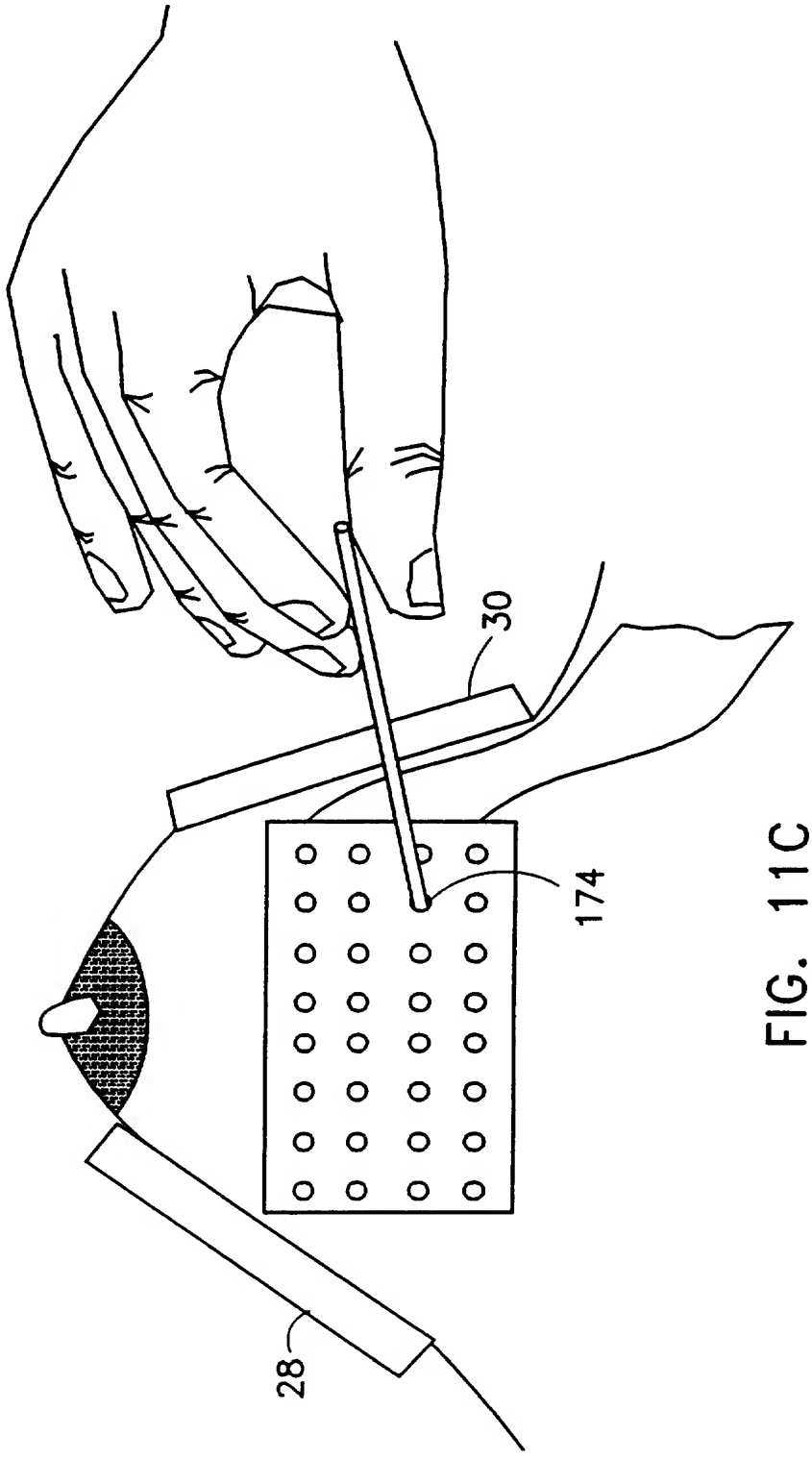
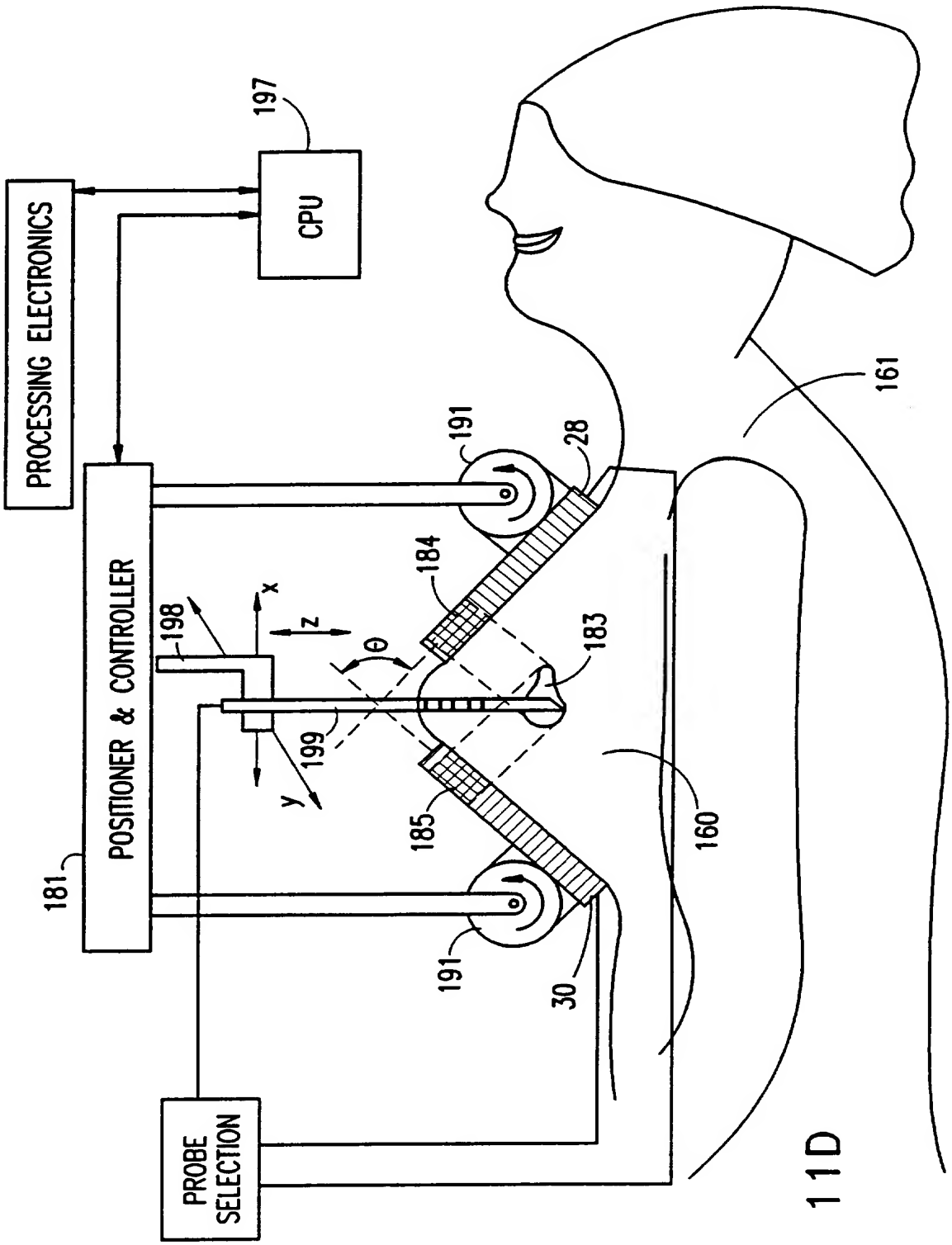


FIG. 11C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POSITIONER & CONTROLLER
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PROBE SELECTION
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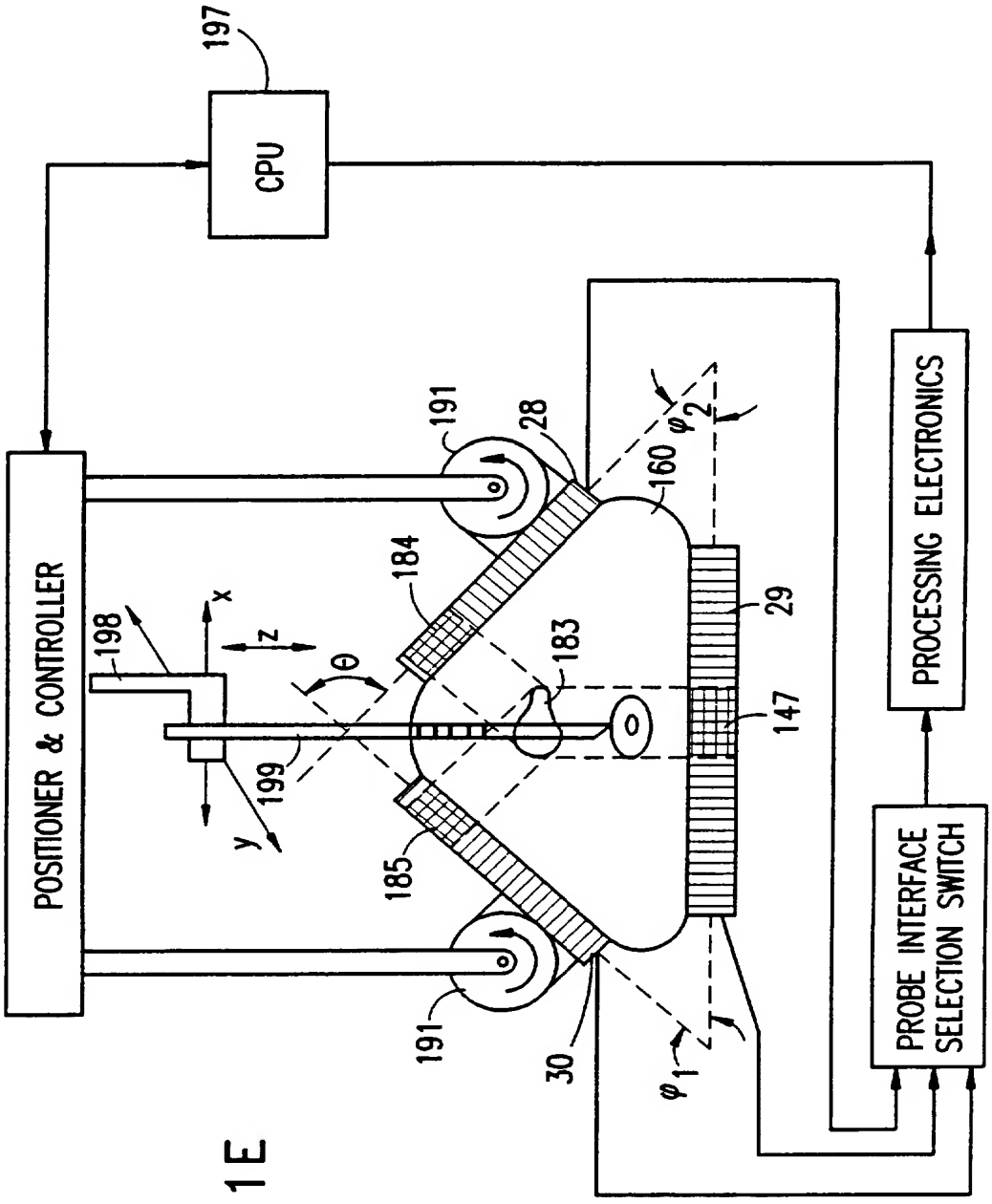
FIG. 11D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y
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191
30
ϕ_1

FIG. 11E

FIG. 12

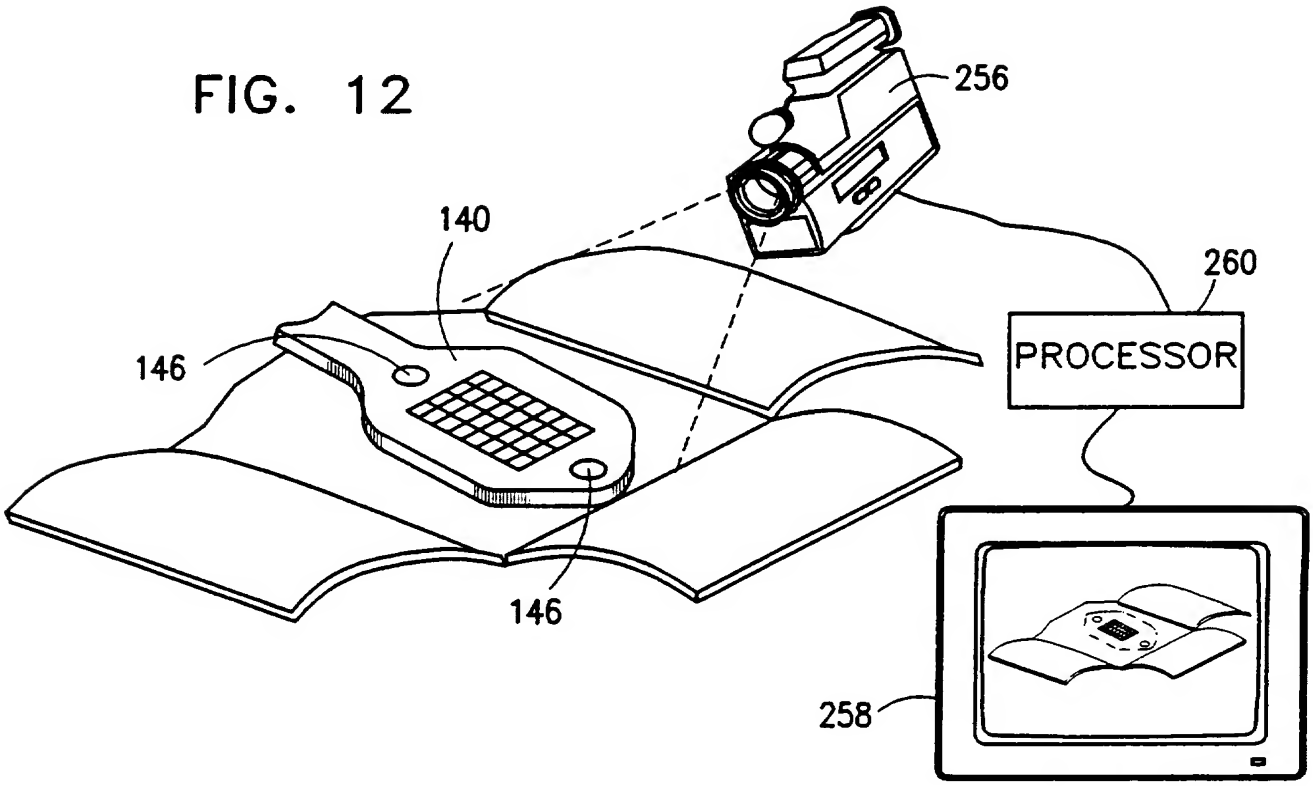
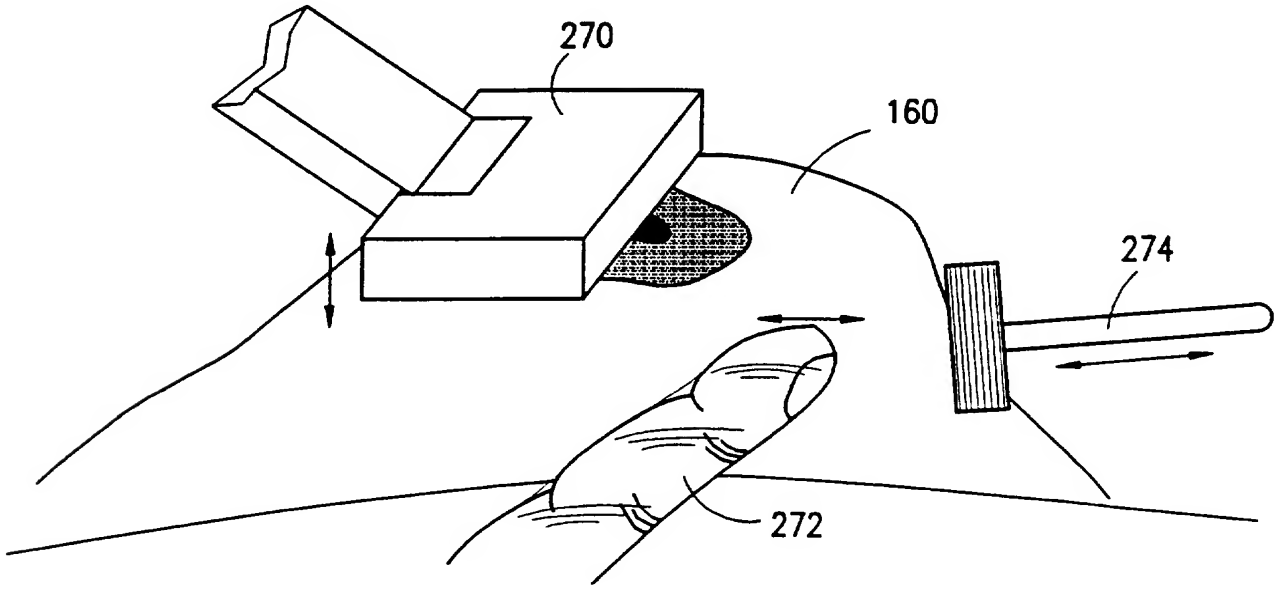


FIG. 16



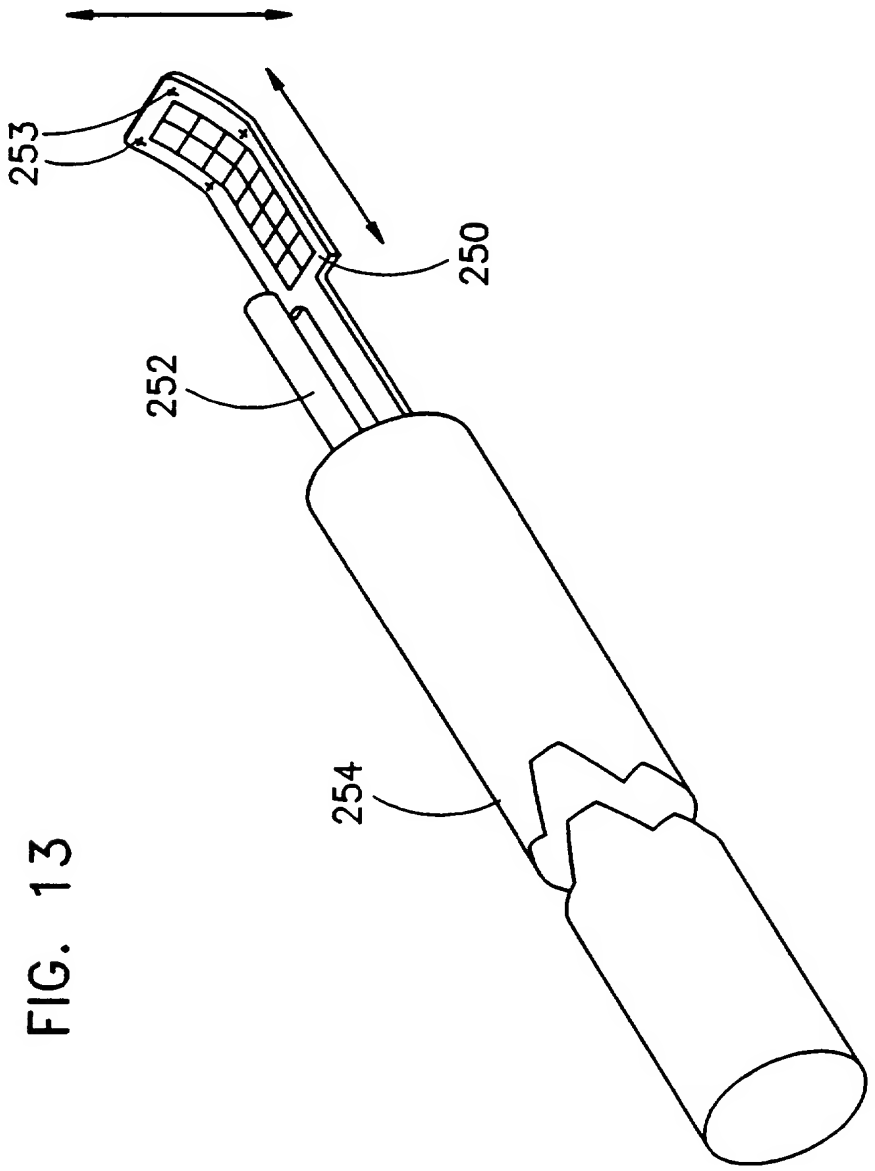


FIG. 13

FIG. 14

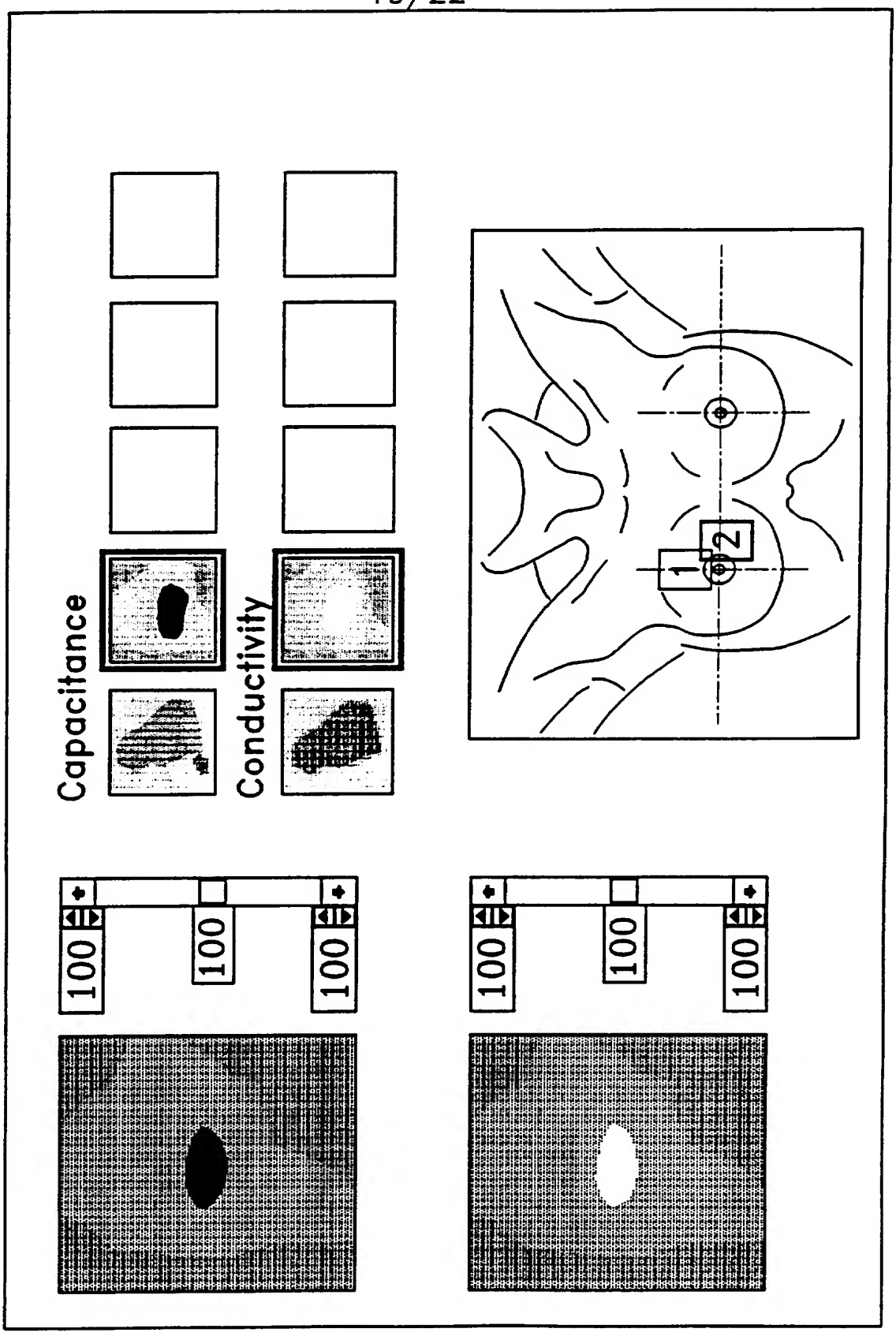
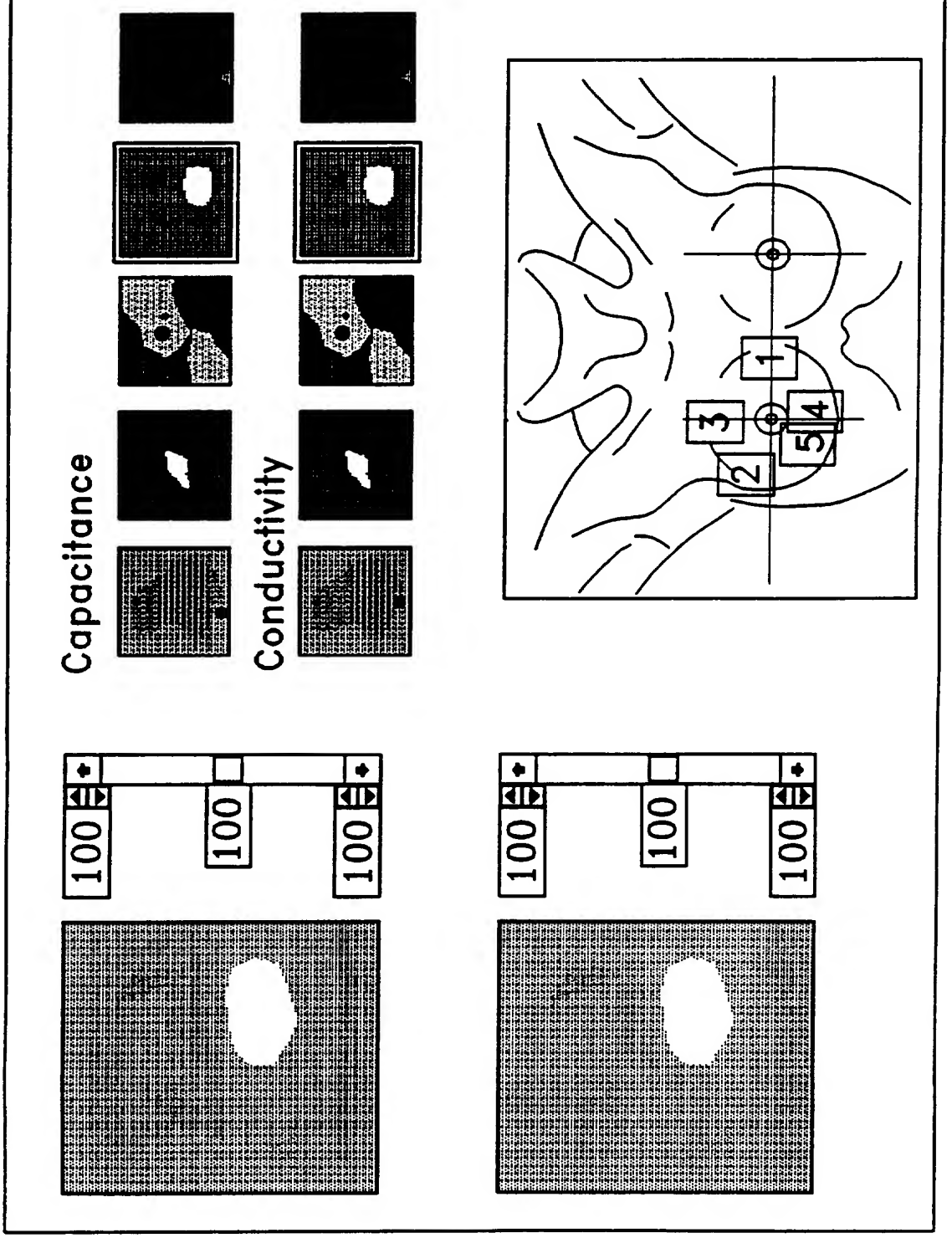


FIG. 15



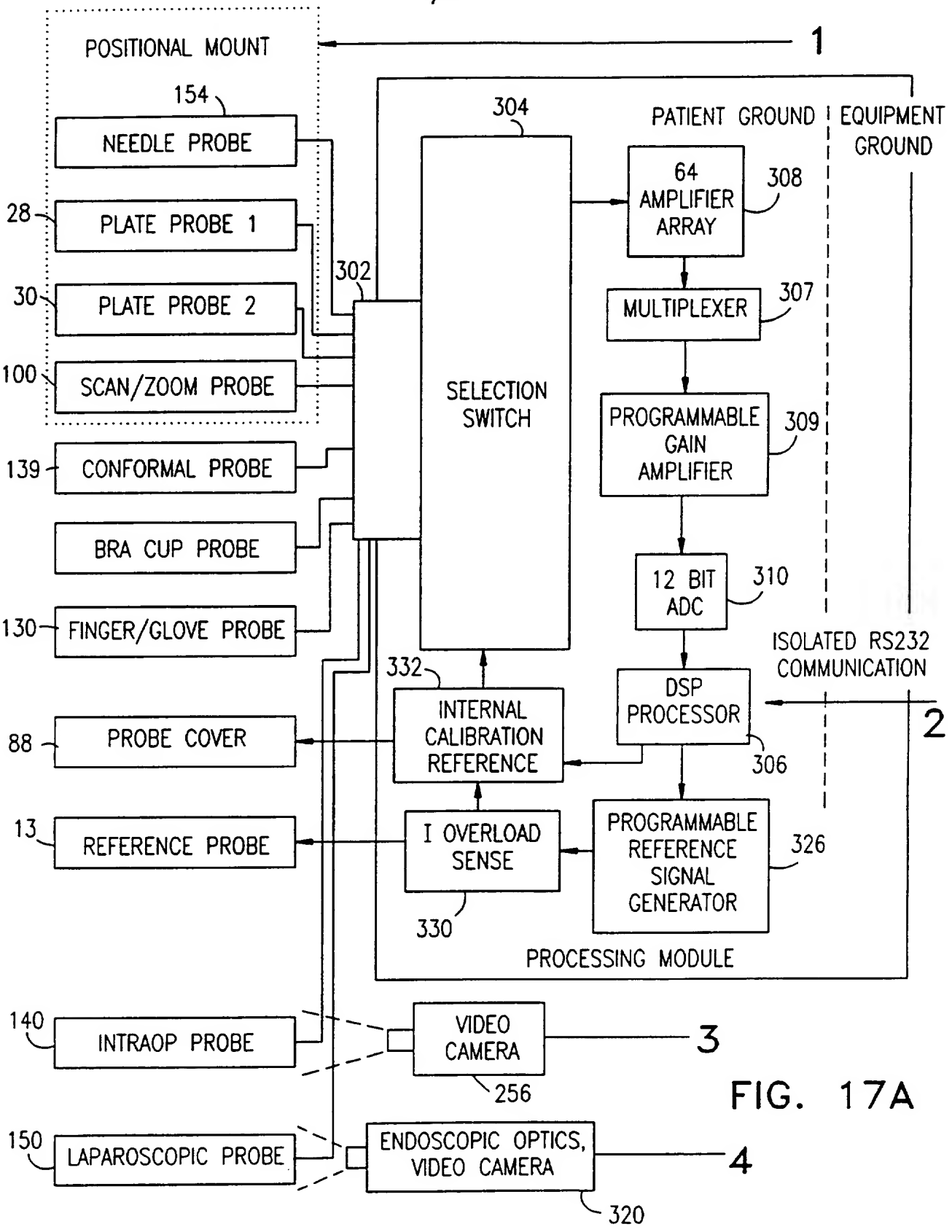

POSITIONAL MOUNT
1
154
NEEDLE PROBE
28
PLATE PROBE 1
30
PLATE PROBE 2
100
SCAN/ZOOM PROBE
139
CONFORMAL PROBE
BRA CUP PROBE
130
FINGER/GLOVE PROBE
88
PROBE COVER
13
REFERENCE PROBE
140
INTRAOP PROBE
150
LAPAROSCOPIC PROBE
302
304
SELECTION SWITCH
PATIENT GROUND
EQUIPMENT GROUND
64 AMPLIFIER ARRAY
308
MULTIPLEXER
307
PROGRAMMABLE GAIN AMPLIFIER
309
12 BIT ADC
310
ISOLATED RS232 COMMUNICATION
DSP PROCESSOR
2
306
332
INTERNAL CALIBRATION REFERENCE
I OVERLOAD SENSE
330
PROGRAMMABLE REFERENCE SIGNAL GENERATOR
326
PROCESSING MODULE
VIDEO CAMERA
3
256
ENDOSCOPIC OPTICS, VIDEO CAMERA
4
320

FIG. 17A

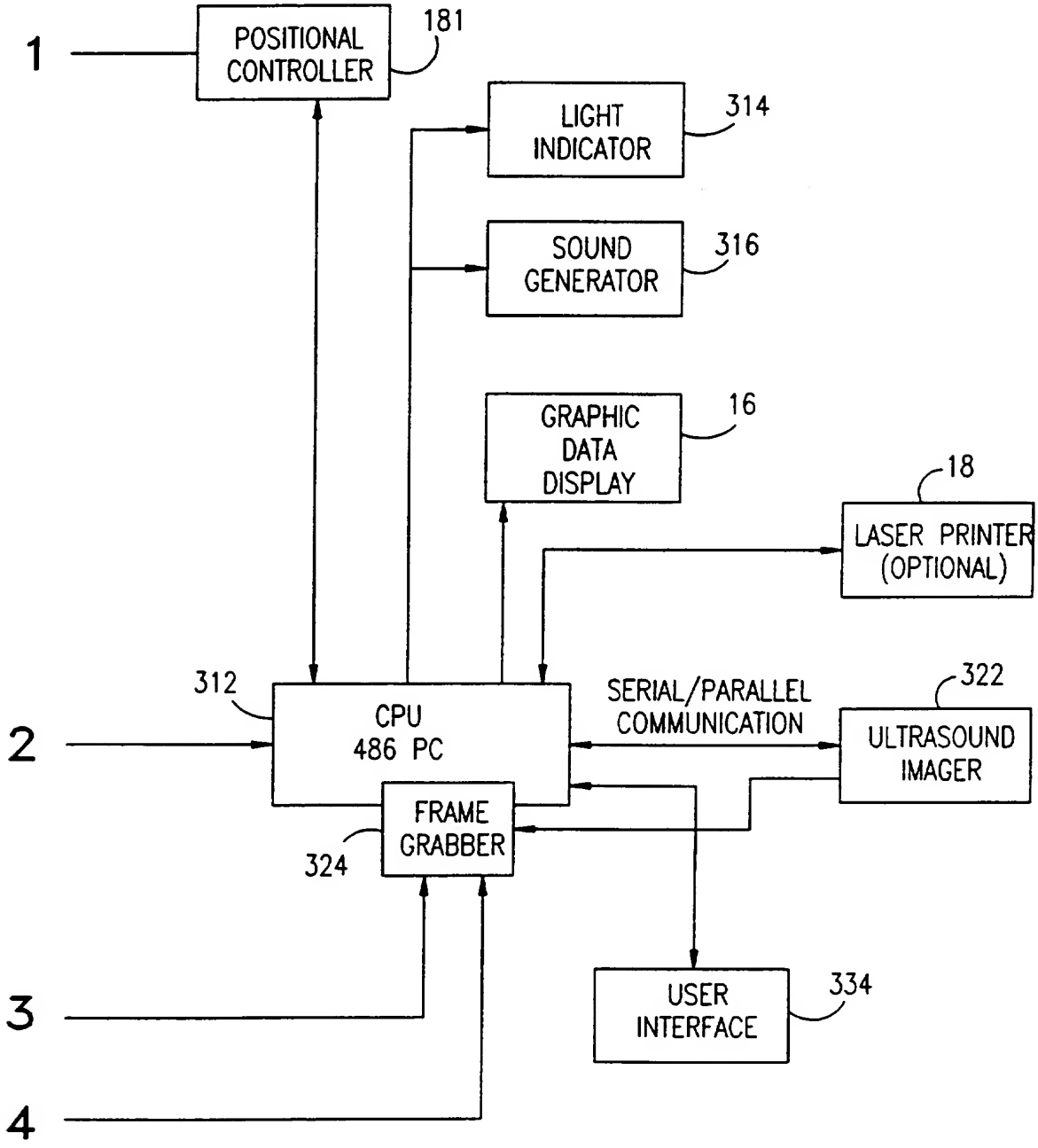

1
POSITIONAL CONTROLLER
181
LIGHT INDICATOR
314
SOUND GENERATOR
316
GRAPHIC DATA DISPLAY
16
18
LASER PRINTER (OPTIONAL)
312
CPU 486 PC
SERIAL/PARALLEL COMMUNICATION
322
ULTRASOUND IMAGER
2
FRAME GRABBER
324
3
USER INTERFACE
334
4

FIG. 17B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06141

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/05
US CL :128/734
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/639, 640, 644, 653.1, 660.01, 660.10, 734, 736

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 5,143,079 (FREI ET AL.) 01 September 1992, see entire document.	1, 5-8, 11, 14-24, 30, 32-35, 37-40, 43-56, 58-62, 68, 70-73, 76, 77
A	US, A, 4,819,658 (KOLODNER) 11 April 1989, see entire document.	1-82
A	US, A, 5,178,147 (OPHIR ET AL.) 12 January 1993, see entire document.	1-82

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be part of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search 21 JULY 1995	Date of mailing of the international search report 07AUG 1995
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer GEORGE MANUEL Telephone No. (703) 308-2118

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